185 TS-ICU
Trauma and Surgical ICU
Kasralainy School of Medicine

2015

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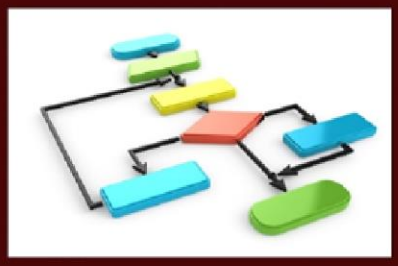

Evidence based
Critical Care protocols

Introduction

There is growing interest in the use of evidence-based clinical practice guidelines as a means of reducing inappropriate care, and making more effective use of health care resources. Moreover a standardized approach to management is desirable for optimal patient care and safety, improving communication and understanding between members of the ICU team and associated specialties.

Critical care protocols should be used as a roadmap for healthcare workers by providing guidance on what is thought to be the best option regarding a specific aspect of care or the consensus on how a given situation is usually best tackled. But they CAN NOT and SHOULD NOT be used in an attempt to replace expert decision-making which weighs up all the aspects of each individual situation.

In the current version of ICU protocols, the management of most frequent critically care problems are illustrated in stepwise approach. More than 50 coloured-flowcharts and tables are added. Each topic ends with a list of references to guide the readers about more resources on the web

Our goal in ***185 New Emergency and Burn Hospital***, is to provide the highest level of patient care, by using ***Evidence-based medicine*** which joins experience-based *practice* in a multidisciplinary approach.

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Admission & Discharge Protocol

Admission Criteria to Intensive Care Unit

Criteria for admission to Intensive Care

1) **Trauma patients**
    a. Injuries
        i. Multisystem trauma
        ii. Severe traumatic brain injuries (GCS<8)
        iii. Cervical spine cord injury
        iv. Severe pulmonary contusion, flail chest
        v. Facial or neck trauma with threatened airway
        vi. Repaired major vascular injuries
        vii. Pelvic fracture with retroperitoneal hematoma
        viii. Blunt cardiac trauma with hypotension or dysrhythmia
        ix. Severe burn (20% TBSA, facial burns)
        x. Isolated high grade solid organ injuries (grade III, IV)
    b. Problems
        i. Respiratory failure requiring mechanical ventilation
        ii. Ongoing shock or hemodynamic instability
        iii. \Massive blood or fluid resuscitation
        iv. Base deficit >5
        v. Hypothermia
        vi. Seizures
        vii. Pregnancy
2) **Post-operative monitoring**
    a. Neurosurgery
    b. major vascular surgery
    c. Long surgical or interventional procedures
    d. massive blood loss

e. Multiple co-morbidities with low systemic reserve)

3) **Postoperative complications:**
    a. Acute respiratory failure requiring Invasive or non-invasive ventilation.
    b. Optimization of fluid balance requiring invasive procedures
    c. Hemodynamic instability requiring inotropic support
    d. Potential for deterioration (e.g. airway swelling, metabolic disorders, coagulopathies, hypoxaemia, hypercarbia, hypovolaemia, intracranial events).
    e. Sepsis with multi-organ dysfunction.
    f. Interventions that cannot be performed in a general ward –continuous veno-venous hemofiltration
4) Preoperative optimization of patients with hemodynamic instability and/or major fluid and electrolyte disturbance
5) Severe acute pancreatitis

Admission Criteria to Intermediate Care Unit

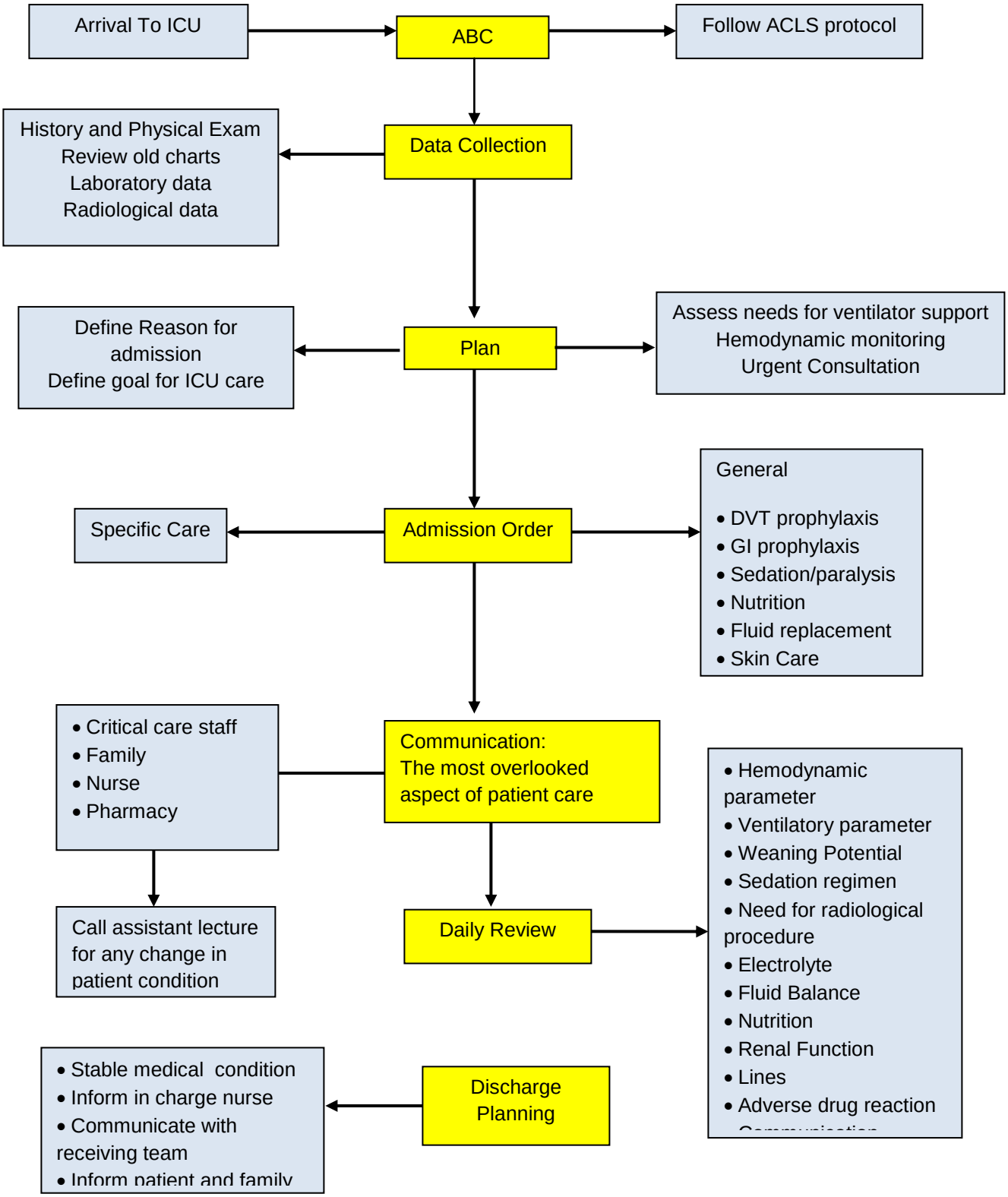
Criteria for admission to Intermediate care
1) Acute traumatic brain injury patients who have a Glasgow Coma Scale above 9 but require frequent monitoring for signs of neurologic deterioration 2) Stable cervical spinal cord injured patients 3) The postoperative patient who, following major surgery, is hemodynamically stable but may require fluid resuscitation and transfusion due to major fluid shifts 4) Appropriately treated and resolving early sepsis without evidence of shock or secondaryorgan failure 5) Hemodynamically stable patients with evidence of compromised gas exchange and underlying disease with the potential for worsening respiratory insufficiency who require frequent observation 6) Diabetic ketoacidosis patients requiring constant intravenous infusion of insulin, or frequent injections of regular insulin during the early

Discharge Criteria

Criteria for discharge from Intensive care unit to ward

1) Patient not on any support or intervention (or unlikely to need them in the next 24 hours) that cannot be provided in the ward. This includes equipment and nurse staffing issues.
2) Low likelihood of deterioration in the next 24 hours. For long-stay patients and those with low systemic reserve, the duration should be extended to 48 hours or more.
3) Supplemental inspired oxygen concentration <50%
4) Hemodynamically stable; any fluid losses should be at a rate manageable in the ward environment
5) Cardiac dysrhythmias are controlled
6) The admission etiological factor is under control or not significant any more
7) Patients in whom treatment has been withdrawn and only need basic nursing care and drugs for comfort

Plan upon admission of patient to ICU



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1. Department of Health Working Group. Guidelines on Admission to and Discharge from Intensive Care and High Dependency Care Units. London:Department of Health. (1996)
2. Daly K, Beale R, Chang S Reduction in mortality after inappropriate early discharge from intensive care unit: logistic regression triage model. Br. Med. J. 2001, 322:1274

Transfer Protocol

Airway • Patients with (or at risk from) airway compromise should be intubated prior to transfer • The tracheal tube should be secured and confirmed in correct position	**Circulation** • Adequate intravenous access • Circulating volume optimized • Hemodynamically stable • All lines are patent and secured • Any active bleeding controlled • Long bone/pelvic fractures stabilized • ECG and blood pressure monitored
C. Spine Adequate spinal immobilization (if indicated)	**Disability** • No active seizures • Initial treatments for raised intracranial pressure (if indicated) • Life-threatening electrolyte disturbances corrected Blood glucose >70 mg/dl
Breathing • Patient adequately sedated if ventilated • Ventilation established (and stable) on transport ventilator • Adequate gas exchange on transport ventilator confirmed by arterial blood gas analysis • Adequate oxygen supply on transfer vehicle	Exposure Patient adequately covered to prevent heat loss

References

1. Intensive Care Society Guidelines for the Transport of the Critically Ill Adult, 2nd edn. London:Intensive Care Society (UK). 2002

Trauma Protocol

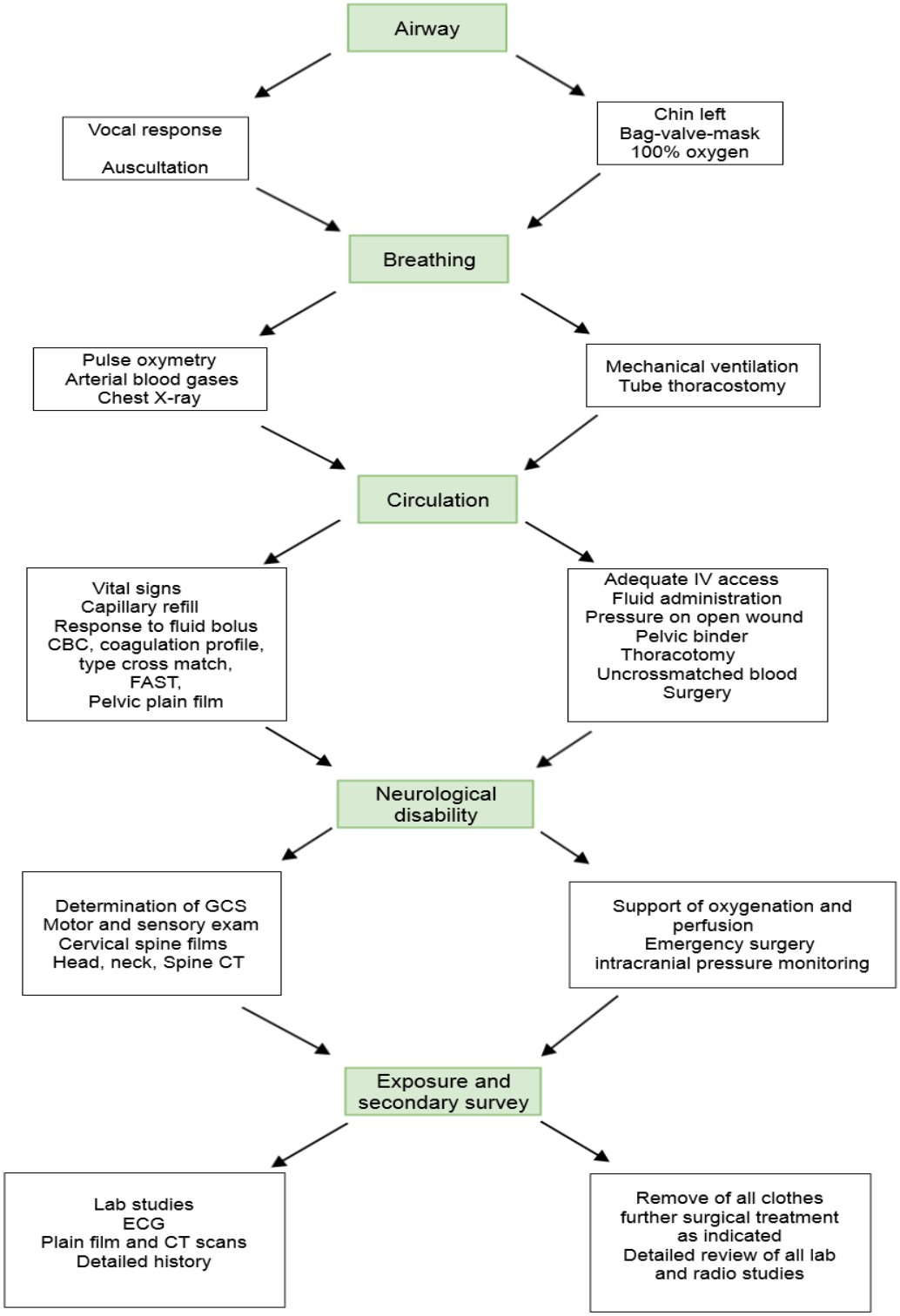

Figure 1: Initial Trauma management

Resuscitation protocol in traumatic hemorrhagic shock

General principle:

- Traumatic death is the main cause of life years lost worldwide. Hemorrhage is responsible for almost 50% of deaths in the first 24 h after trauma.
- The optimal resuscitative strategy is controversial: choice of fluid for resuscitation, the target of hemodynamic goals for hemorrhage control, and the optimal prevention of traumatic coagulopathy are questions that remain.

Fluid resuscitation

I. Type of fluid

- Lactated Ringer's solution is recommended as first-line resuscitation fluid in trauma patients
- Albumin should be avoided in patients with TBI
- In patients with TBI, isotonic saline should be preferred over hypotonic fluids because it can reduce the risk of cerebral edema.

II. Endpoints of resuscitation

- Three different target systolic blood pressure values can be considered for three different traumatic conditions before controlling source of hemorrhage:
  - 60–70 mmHg for penetrating trauma
  - 80–90 mmHg for blunt trauma without TBI
  - 100–110 mmHg for blunt trauma with TBI
- Lactate ≥ 2 mmol/L and base deficits ≥ -5 mEq/L have been demonstrated useful to stratify patients who need a larger amount of fluid after the initial resuscitation.

III. Vasopressor

- Early use of norepinephrine could limit fluid resuscitation and hemodilution.
- The dose of norepinephrine should be titrated until we reach the target systolic blood pressure as indicated above

IV. Transfusion and prevention of acute coagulopathy of trauma

The correction and prevention of traumatic coagulopathy have become central goals of early resuscitative management of hemorrhagic shock.

a) Red blood cells

- In patients without TBI: Target haemoglobin level (7-9 g/dL)
- In patients with severe TBI (GCS ≤ 8): Target haemoglobin level ≥ 10 g/dL

a) Fresh Frozen Plasma (FFP)

- In all patients FFP should be considered when PT or PTT ≥ 1.5 times normal value

- The initial recommended dose of FFP is 10 to 15 ml/kg

b) Platelet

- In patients without TBI: Platelet transfusion is recommended when platelet count ≤ 50.000/L
- In patients with TBI: Platelet transfusion is recommended when platelet count ≤ 100.000/L

c) Fibrinogen

- In all patients, fibrinogen level should be maintained ≥ 150-200 mg/dL
- The use of FFP failed to rapidly correct the hypofibrinogenemia
    - Resuscitation with 10 to 15 mL/kg of FFP only increased the fibrinogen plasma level to 40 mg/dL
    - More than 30 mL.kg of FPP should be necessary to increase the fibrinogen plasma level to 100 mg/dL
- 10 single bags of cryoprecipitate derived from whole blood are needed to raise the plasma fibrinogen level by 100 mg/dL

d) Adjuvant Therapy

I. Tranxemic acid: routine administration of tranexamic acid (loading dose of 1 g over 10 min, then infusion of 1g over 8 hr) in patients with hemorrhagic shock was associated with a decreased mortality rate.

II. Factor VIIa: No clear recommendation to use activate factor VII and the use of this factor should be discussed on a case-by-case basis.

III. Ionized calcium level should be maintained between 1.1-1.3 mmol/L

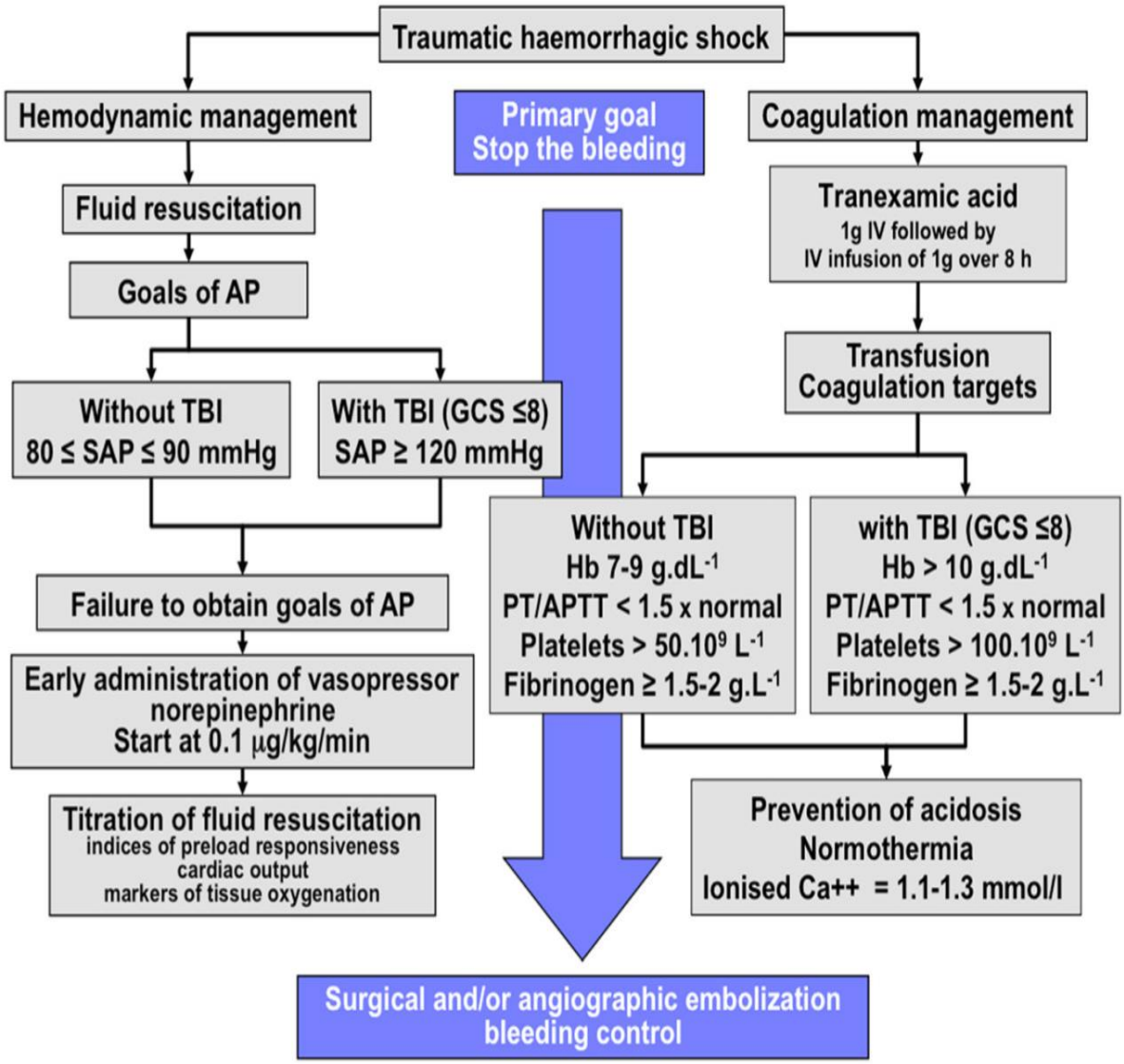

Figure 2: initial management of traumatic hemorrhagic shock [1]

References

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Traumatic Brain Injury

General principle

- Traumatic brain injury (TBI) is a serious public health problem in Egypt, contributing to over 50% of trauma deaths
- Protocolized management of severe TBI [defined as a post-resuscitation Glasgow Coma Score (GCS) < 8] has been demonstrated to improve patient outcome
- Protocol for management of TBI is based on management guidelines proposed by PROTECT III trial

Resuscitation and basic physiologic goals

A. Airway management

- Patients with a GCS ≤ 8 should be intubated for airway protection
- Sedative and analgesic choices should include short acting agents through the initial resuscitation, as temporal assessment of neurological status is critical
    - Propofol is strongly recommended as the choice for sedation,
    - Succinylcholine, Rocuronium bromide – paralytic for induction

B. Oxygenation/Ventilation

- The Target Oxygen status is PaO2 ≥ 100 mmHg and O2 Sat ≥ 90%
- Avoidance of hypoxia
    - Patients with moderate TBI who do not require intubation should have pulse oximetry maintained to at least 90%.
    - Intubated patients PaO2 should be maintained at ≥ 100 mmHg, except during weaning. Pulse oximetry > 90 % remains goal during ventilation wean
- Ventilation
    - Hyperventilation should be intensively avoided during the initial resuscitation
    - The Target PaCO2 is (35-45 mmHg)
    - Prophylactic hyperventilation (PaCO2 < 35 mmHg) is prohibited.
    - Therapeutic hyperventilation may be necessary for brief periods when there is acute neurological deterioration that coincides with a cerebral herniation syndrome or for refractory elevations in ICP

C. Blood Pressure, Volume Resuscitation, Anemia, and Coagulopathy

- Blood Pressure
    - A systolic blood pressure (SBP) should be kept between 100 mmHg and 180 mmHg. Recognize that lower blood pressures can represent a “relative” hypotensive state in TBI patients (especially with elevated ICP)

- Normal Saline Fluid should be used as the initial method of maintaining euvolemia to achieve the target blood pressure.
- Assessment for transfusion and/or implementation of vasoactive drugs should be considered for treatment of hypotension. Such Vasopressors or Inotrops include Phenylephrine (Neosynephrine), Levophed, Epinephrine, Dobutamine, and Vasopressin.

- Euvolemia – The primary target is euvolemia.
  - In many cases a central venous pressure (CVP) monitor will be placed. A CVP goal of 5-7 mmHg correlates with euvolemia, but should be assessed in the context of the individual patient's clinical picture. CVP or other types of invasive monitoring are recommended in patients with severe TBI requiring ventriculostomy or intubation.
  - Brain-injured patients should be maintained in a euvolemic state with volume replacement of blood products and crystalloid.
  - The initial resuscitation fluid should be normal saline. Hypertonic saline should only be used as a secondary osmotic agent in ICP control.
  - Volume resuscitation to achieve euvolemia should NOT be withheld to prevent concerns with cerebral edema.
  - Conversely, hypervolemia should be avoided as it is associated with increased incidence of ARDS in TBI patients.
- Anemia - The target is to keep hemoglobin concentration at 8 g/dl or above.
  - The hemoglobin concentration (Hgb) of the patient should be maintained at ≥ 8 g/dL
  - Blood should be transfused for Hg < 8 g/dL.
- Coagulation – Coagulation panels should be followed closely.
  - The Target INR is less than or equal to 1.4
  - FFP, Vitamin K, Factor VII, should be administered, as clinically indicated, in order to correct coagulopathy.
  - INR and platelet count should be corrected in anticipation of placement of ventriculostomy, or other intracranial surgery.
  - Platelets should be transfused for a platelet count < 75 x 10^3 / mm^3.

Intracranial Pressure (ICP) Monitoring

- All patients with signs and symptoms of increased intracranial pressure (ICP) and/or GCS ≤ 8 should receive a ventriculostomy for ICP monitoring (unless there is a direct contraindication to invasive monitoring, such as INR >1.4 or platelet count of <75 x 10^3

Indications

- Salvageable patients with severe TBI (GCS 3-8 after resuscitation) and an abnormal CT scan (hemorrhage, contusions, swelling, herniation or compressed basal cisterns)
- Patients with severe TBI and normal CT scan if two of the following are noted at admission: age > 40 yrs, unilateral or bilateral posturing, systolic BP < 90 mmHg

Management of increased ICP

- General recommendation
  - Ventilation – Keep O2 Sat >90, and PaO2>100, and PCO2 = 35-45.
  - Monitor Systolic BP and MAP - avoid hypotension, Systolic >100 mmHg.
  - Normothermia goal <38.3°C: treat fever with acetaminophen and/or cooling blankets.
  - Adjust cervical collar placement if applicable.
  - Consider repeat CT: a repeat CT scan of the brain should be considered to rule out the development of a surgical mass or unexpected intracranial lesion
- TIER 1
  - Head of patient's bed to be placed at ≥ 30 degrees.
  - Sedation and analgesia using recommended agents (propofol, fentanyl, and versed) in intubated patients. Pain relief and sedation are appropriate initial modalities for treatment of intracranial hypertension.
  - Ventriculostomy - extraventricular drain; drain to 10 cmH2O for ICP ≥ 20 mmHg sustained for ≥ 5min
  - Mannitol – 0.25-1.0g/kg; IV bolus x 1 dose

  Tier 1 completed within 120 minutes, if ICP ≥ 20 mmHg/27.2 cm H20 mmHg proceed to Tier 2

- TIER 2
  - Hyperosmolar therapy
    - Mannitol: intermittent boluses of mannitol (0.25 - 1 gm/kg body weight) should be administered.
    - Hypertonic saline: boluses of 3% sodium chloride solution (250 cc over ½ hour)
    - Measure serum osmolality and electrolytes q 12 hrs
    - Hold hypertonic saline therapy for serum Na > 160 mEq/L
    - Hold mannitol therapy for serum osmolality > 320 mOsm
  - Protect the Brain
    - Initiate continuous EEG monitoring to rule non-convulsive status epilepticus
    - Provide judicious analgesia and sedation to control pain and agitation
      - Fentanyl 25-150 mcg/hr IV infusion
      - Propofol 10-50 mcg/kg/hr IV infusion for Richmond Agitation Sedation Score (RASS) > -2

Tier II completed within 120 minutes, if ICP ≥ 20 cmH20/mmHg proceed to Tier 3.

- TIER 3
    - Decompressive hemi-craniectomy or bilateral craniectomy should only be performed if Tiers 1 and 2 are not sufficient.
    - Barbiturate
        - Pentobarbital 10 mg/kg IV over 10 minutes, then 5 mg/kg IV q 1 hr x 3, then 1 mg/kg/hr IV infusion
        - Titrate pentobarbital to the minimal dose required to achieve EEG burst suppression
        - Discontinue all other sedative agents and paralytics

Adjunctive Medication and prevention of complication

A. Antiseizure Prophylaxis

- Post traumatic seizures are a recognised complication of closed head injuries with incidence depending largely on severity of injury.
- Post traumatic seizures are classified as either
    - Immediate, early (0-7 days) or
    - Late/delayed (>7 days)
- Anti-convulsants are therefore only indicated in the first week following closed head injury to reduce the risk of complications from early post traumatic seizures. They should not be routinely continued long term.
- The following CT scan findings may indicate the need for late PTS prophylaxis (anticonvulsant therapy for longer than 7 days post injury) (1):
    - Biparietal contusions.
    - Dural penetration with bone and metal fragments.
    - Multiple intracranial operations.
    - Multiple subcortical contusions.
    - Subdural hematoma with evacuation.
    - Midline shift greater than 5mm.
    - Multiple or bilateral cortical contusions.
- Anticonvulsant drugs
    - Phenytoin is effective in decreasing the risk of early PTS in patients with severe TBI.
        - Dose: phenytoin is administered intravenously with a loading dose of 17 mg/kg intravenous infusion over 30-60 minutes, followed by a maintenance dose of 100 mg given three times daily, either intravenously or orally for a total of seven days.
        - Valproate should **NOT** be used for early PTS prophylaxis.
        - Levetiracetam is an effective and safe alternative to phenytoin for early PTS prophylaxis.

- Dose: A loading dose of 20 mg/kg IV (rounded to the nearest 250 mg and administered over 60 min) followed by a maintenance dose of 1000 mg IV every 12 hrs (given over 15 min)

B. Glucocorticoids

- The use of glucocorticoids is not effective at improving outcome or reducing intracranial hypertension, and should **NOT** be administered

C. Stress Ulcer Prophylaxis

- Patients with significant traumatic brain injury requiring mechanical ventilation as well as those with coagulopathies or a history of gastric or duodenal ulcers should receive stress ulcer prophylaxis

D. Deep Venous Thrombosis (DVT) Prophylaxis

- All patients with significant traumatic brain injury requiring mechanical ventilation and sedation should receive DVT prophylaxis in the form of sequential compression stockings upon admission
- Subcutaneous low-dose heparin may also be initiated within 72 hours of admission, unless contraindicated due to evidence of bleeding, need for surgery, or indwelling intracranial monitor.

E. Early Tracheostomy

- Tracheostomy is recommended in ventilator dependent patients to reduce total days of ET intubation.

Metabolic Monitoring

A. Serum Electrolyte

- The baseline goal for electrolytes (such as, sodium) will be to maintain within normal range (Na 135-145 mmol/L)
- In the treatment of elevated ICP with HTS, Na goal increases to a target of 145 mmol/L (lower threshold) and 160 mmol/L (upper threshold).

B. Glucose Monitoring

- The glucose level should be maintained between 80 and 180 mg/dl.
- Serum glucose should be monitored frequently following the initiation of nutritional support, particularly in patients with known or suspected diabetes mellitus.
- In the ICU, initial treatment with regular insulin for hyperglycemia is recommended, with subsequent transition to other patient specific regimens per team.

Nutritional Support

- Nutritional support should be initiated via gastric or enteral route within 72 hours post injury

- Frequent assessment of residual volumes of gastric nutrition should be performed, as patients with TBI frequently do not tolerate intragastric feeding, and are at risk for emesis and aspiration.
- TPN should be utilized cautiously in patients with TBI due to the high glucose concentrations of hyperalimentation solutions

NON-Emergency Surgery

- Non-Emergent surgeries that require general anesthesia, such as orthopedic procedures and plastic surgery, should be avoided in **BOTH** moderate and severe TBI patients until it is clear that the brain injury has stabilized or resolved.
- In the case of Emergency surgeries, priority should be given to maintaining target physiological parameters such as systolic blood pressure > 100 mmHg (or higher if ICP is elevated), and oxygenation ($PaO_2 \geq 100$ mmHg and Pulse Ox ≥ 90%) in all patients suspected of having a TBI.

SURGICAL MANAGEMENT OF TBI

A. Epidural Hematomas

- Epidural hematoma should be surgically evacuated if
  - epidural hematoma (EDH) of greater than 30 cm^3
  - acute EDH, GCS <9, and anisocoria
- EDH of less than 5 mm midline shift in patients with GCS >8 and no focal neurological deficit can be closely monitored in an ICU with serial CT scans

B. Acute Subdural Hematomas

- Acute subdural hematomas (SDH) should be evacuated emergently if
  - (SDH) with a thickness of greater than 10 mm or 5 mm of midline shift on CT scan regardless of the GCS
  - SDH less than 10 mm thickness and less than 5 mm midline shift should be evacuated emergently if the patient has: GCS decrease by 2 points, asymmetric pupils or fixed pupils, or ICP > 20 mmHg

C. Subarachnoid Hemorrhage

- All patients with GCS <9 and SAH should have a ventriculostomy inserted.

D. Parenchymal Lesions

- Intraparenchymal hemorrhage (IPH) should be evacuated if
  - medically refractory ICP elevations, or significant mass effect
  - Frontal or temporal contusions with IPH >20 cm3 and >5 mm shift or cistern compression in patients with GCS 6-8
  - IPH >50 cm3

E. Diffuse Medically-Refractory Cerebral Edema and Elevated ICP

- Decompressive craniectomy for refractory elevated ICP (unilateral or bilateral) within 48 hours of injury is an option in TIER 3

F. Posterior Fossa Mass Lesions

- Patients with posterior fossa (PF) lesions that show distortion, dislocation, or obliteration of the 4th ventricle, or compression or loss of visualization of the basal cisterns, or obstructive hydrocephalus on CT should be evacuated

G. Depressed Skull Fractures

- Open skull fractures depressed greater than the thickness of the inner and outer table should undergo operative management.
- Open depressed fractures that are less than 1cm depressed and have no dural penetration, no significant intracranial hematomas, no frontal sinus involvement, no gross cosmetic deformity, no pneumocephalus, and/or no gross wound contamination may be managed non-operatively
- All open skull fractures should be treated with prophylactic IV antibiotics, such as Vancomycin and Ceftriaxone.

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1. Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, Joint Section on Neurotrauma and Critical Care. Guidelines for the Management of Severe Traumatic Brain Injury J Neurotrauma 2007;24:1-106.
2. Stevens RD, Huff JS, Duckworth J, Papangelou A, Weingart SD, Smith WS. Emergency neurological Life Support: Intracranial Hypertension and Herniation. Neurocrit Care 2012; 17:S60-S65.
3. Debenham S, Sabit B, Saluja RS, Lamoureux J, Bajsarowicz P, Maleki M, Marcoux J. A critical look at phenytoin use for early post-traumatic seizure prophylaxis. Can J Neurol Sci. 2011; 38:896-901

Acute Spinal Cord Injury

A. Initial assessment

- Airway
- Breathing
- Circulation
- Disability
- Exposure

B. Radiographic assessment

- Radiographic evaluation of the cervical spine is not recommended in
    - Awake, asymptomatic patient who is without neck pain or tenderness.
    - Who has normal neurological examination, is without an injury detracting from an accurate evaluation,
- High-quality computed tomography (CT) imaging of the cervical spine is recommended in.
    - The awake, symptomatic patient
    - The obtunded or unevaluable patient
- If high-quality CT imaging is not available, a 3-view cervical spine series (anteroposterior, lateral, and odontoid views) is recommended

C. Cardiopulmonary management

- Correction of hypotension in spinal cord injury (systolic blood pressure, 90 mmHg) when possible and as soon as possible is recommended.
- Correction of hypotension can be done by
    - NS 2L IV – only for trauma bay resuscitation
    - Norepinephrine 0.05mcg/kg/min – titrate to keep MAP >70
    - Consider Midodrine 5mg po TID

D. Gastrointestinal management

- Stress Ulcer Prophylaxis: PPI 20mg IV/ Q12H VTE prophylaxis
- Obtain feeding access and initiate enteral support within 48 hours
- Maintain normoglycemia (Blood Glucose < 180)

E. Pharmacologic treatment

- Administration of methylprednisolone (MP) for the treatment of acute spinal cord injury (SCI) **IS NOT** recommended.

References

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Hemodynamic Assessment of Patients with Circulatory failure

Hemodynamic monitoring can only improve outcomes if three conditions are met:

1. The data obtained from the monitoring device must be sufficiently accurate to be able to influence therapeutic decision making
2. The data obtained from the monitoring system must be relevant to the patient being monitored
3. The changes in management made as a result of the data obtained need to be able to improve outcomes.

The approach asks three sequential questions before giving any treatment.

1. Is the patient hemodynamically unstable? Is there sign of tissue hypoperfusion?
    a. MAP <65 mm Hg, a decrease in MAP of > 20 mm Hg in a previously hypertensive patient and one of the two (b and c below)
    b. Evidence of end-organ hypoperfusion: a decrease in urine output to <20 ml/hr, confusion, new onset tachycardia, lactic acidosis, ileus
    c. Symptoms of increased sympathetic tone: agitation, confusion, restlessness
2. Is the patient preload-responsive?
    a. For initial evaluation of the critically ill patient, an invasive approach is still often needed, which includes insertion of an arterial catheter and a central venous catheter
    b. Inferior Vena Cava (IVC) can be used to provides an indication of intravascular volume and has been used to estimate the central venous pressure (CVP) (**IVC collapsibility index**)
        i. IVC diameter <2.1 cm that collapses >50% with sniff correlates to a CVP pressure of 3 mm Hg (range 0–5 mm Hg)
        ii. A larger IVC >2.1 cm that collapses <50% suggests a high CVP pressure of 15 mm Hg.
        iii. IVC collapsibility index **(max-min)/ max** value). This index is used only for **spontaneously breathing non ventilated** patients
    c. In patients with normal to high CVP or larger IVC diameter and or IVC <2.1 with low collapsibility, dynamic tests should be used to detect fluid responsiveness.
        i. In mechanically ventilated patients with tidal volume of 6-8 ml/kg with no significant arrhythmia.
            1. Pulse pressure variation (PPV) refers to the difference between the maximum (PP_{max}) and minimum (PP_{min}) pulse pressure over a single mechanical breath. A PPV of ≥13% has been shown to be a specific and sensitive indicator of preload responsiveness. (Fig. 1)

$$\mathbf{PPV\% = 100 \times \{(PP_{max} - PP_{min}) / (PP_{max} + PP_{min})/2\}}$$

2. IVC distensibility index **(max-min)/min value)** > 18%

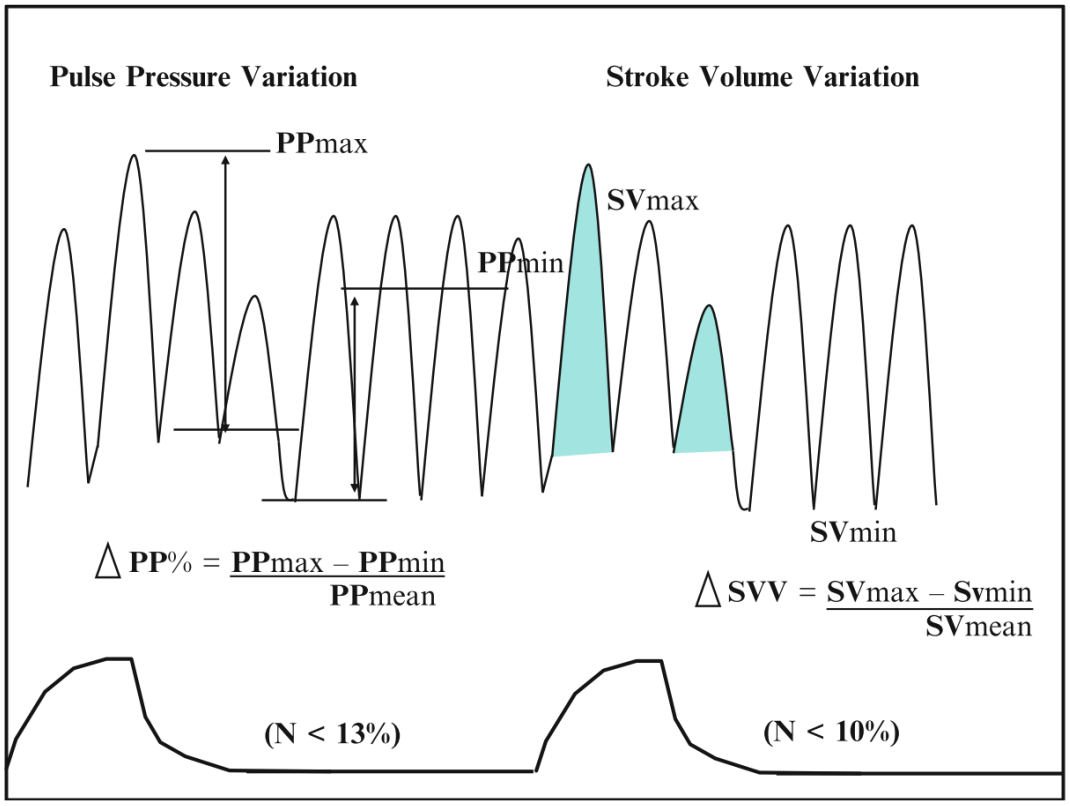

Figure 3: Pulse pressure variation and stroke volume variation

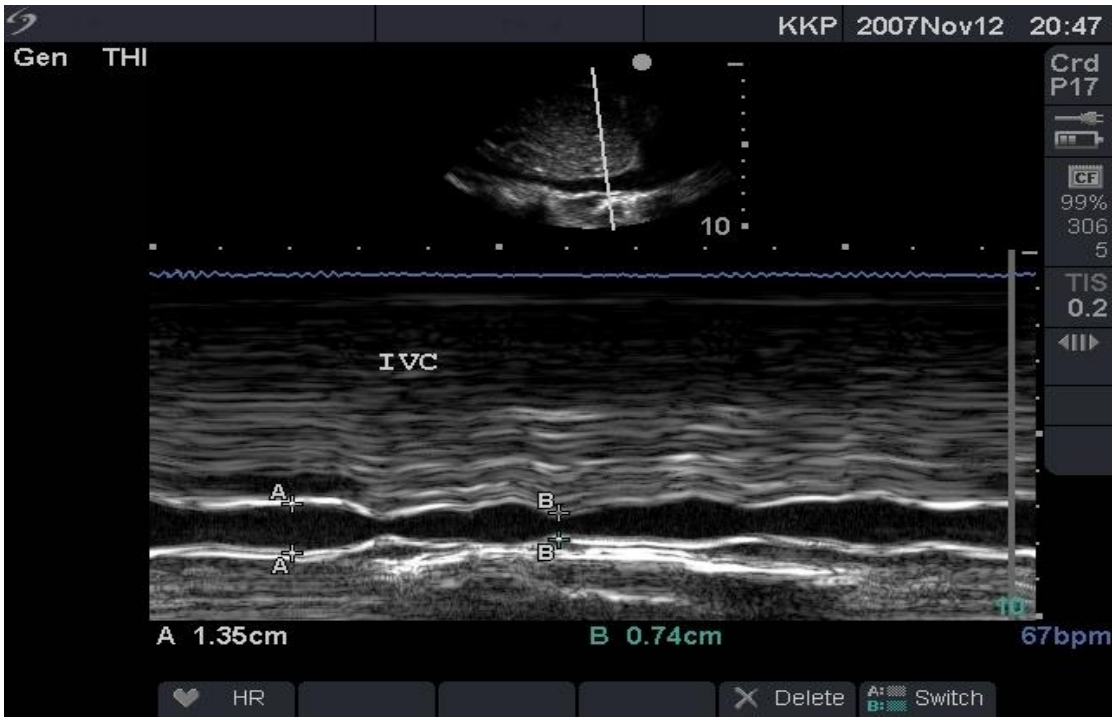

Figure 4: Measuring the maximum and minimum diameters in a M-mode tracing of the IVC

ii. In spontaneously breathing patient, or the presence of significant arrhythmia
    1. Passive leg raising test (PLR) together with measuring SV by Doppler or VTI by transthoracic echo TTE. Increase these indices by 15% or more indicate fluid responsiveness. (Fig 2)

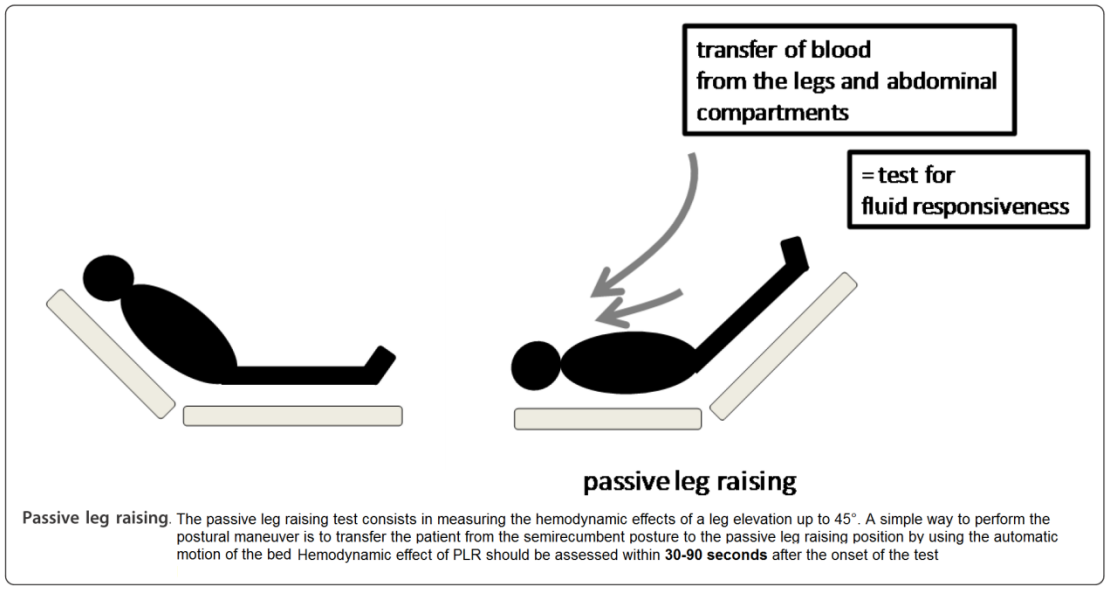

Figure 5: Leg raising test

3. What is the status of cardiac function? (Figure 3)
    a. Evaluation for the presence of pericardial effusion and cardiac tamponade.
        i. The first step is to visualize pericardial sac to determine if the patient has a pericardial effusion.
        ii. If a pericardial effusion is identified, the next step is to evaluate the heart for signs of tamponade. Evaluation for cardiac tamponade specifically focuses on the movement of the right atrium and ventricle during diastolic filling.
    b. Evaluation of Left Ventricular Contractility
        i. The left ventricle can be analyzed for global contractility in left parasternal long axis and short axis view
        ii. Based on these assessments, a patient's contractility can be broadly categorized as being normal, mild-moderately decreased, or severely decreased.
    c. Evaluation of Right Ventricular Size
        i. Evaluation of right ventricular size in left parasternal long axis view, apical 4 chamber view, and/or subxiphoid view
        ii. Signs of higher pressures within the right side of the heart and the pulmonary artery include:
            1. Dilation of the right ventricle, especially to a size equal to or greater than the left ventricle
            2. Deflection of the inter-ventricular septum toward the left ventricle

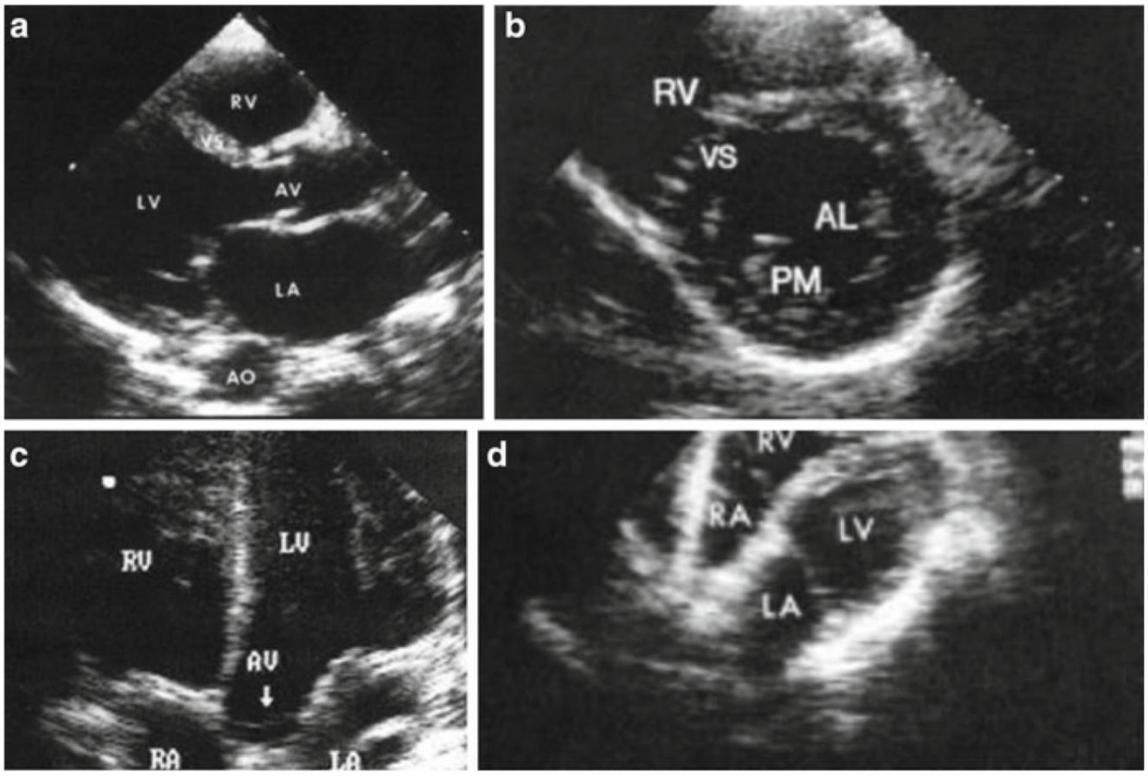

Figure 6: Four basic echocardiographic views:

(a) left parasternal long axis, (b) left parasternal short axis, (c) apical four chambers, and (d) subcostal

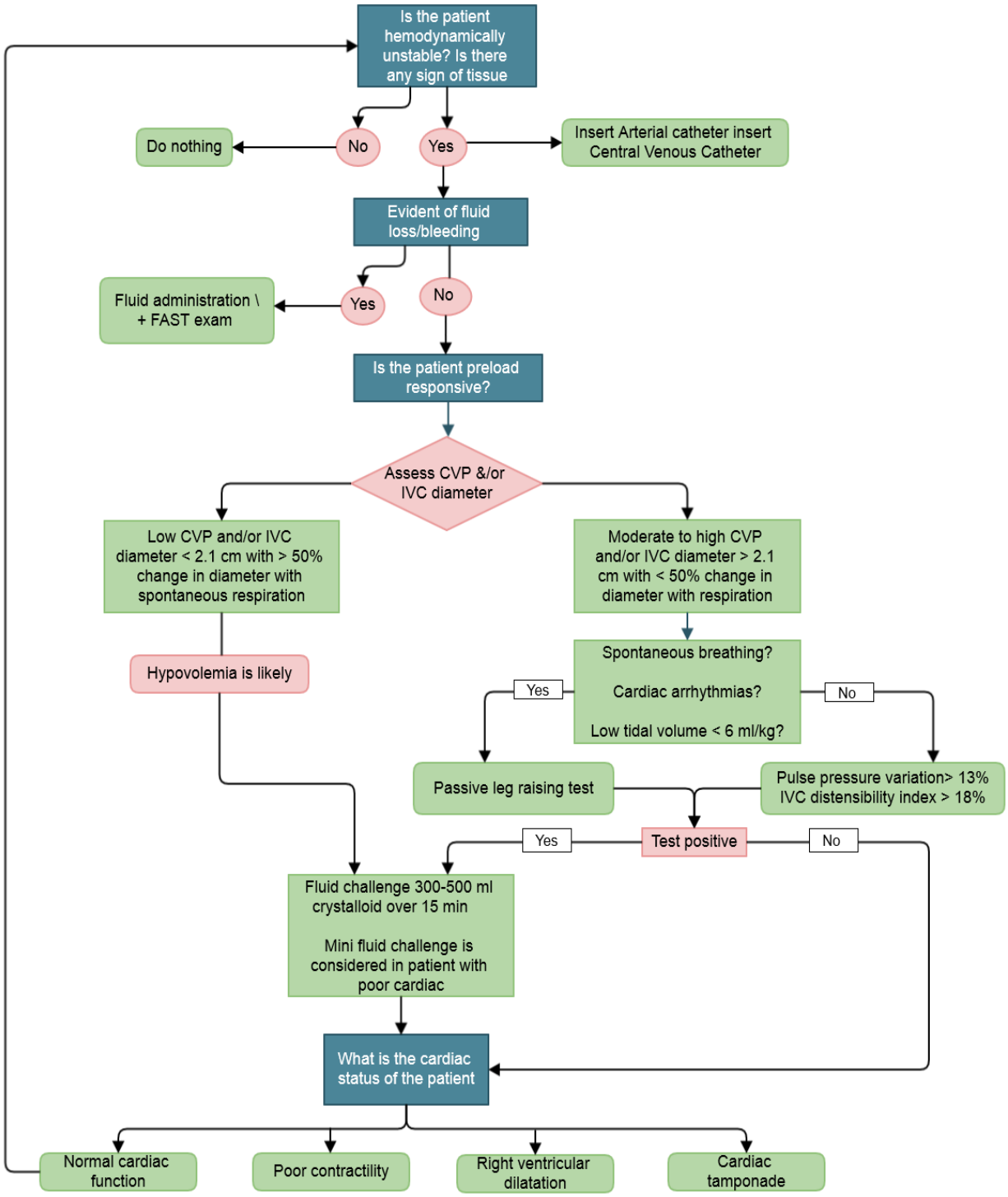

Figure 7: Stepwise approach of assessment of hemodynamically unstable patient

References

1. Monnet X, Teboul JL. Assessment of volume responsiveness during mechanical ventilation: recent advances. Crit Care. 2013;17:217
2. Seif D, Perera P, Mailhot T. Bedside ultrasound in resuscitation and therapid ultrasound in shock protocol. Crit Care Res Pract.2012;2012:503254.
3. Vincent JL, Rhodes A, Perel A. et al. Clinical review: Update on hemodynamic monitoring--a consensus of 16. Crit Care. 2011;15:229

Sepsis Management Protocol

General principles

- Treatment guidelines follow those recommended by the Surviving Sepsis Campaign
- Definitions:
    - *SIRS (Systemic inflammatory response syndrome):* The clinical syndrome that results from a deregulated inflammatory response or to a noninfectious insult.
    - *Sepsis:* SIRS that is secondary to infection that has been diagnosed clinically. Positive cultures add to the validity but are not required for the diagnosis.
    - *Severe Sepsis:* Sepsis plus at least one sign of hypoperfusion or organ dysfunction (see below), that is new, and not explained by other known etiology of organ dysfunction.
    - *Septic Shock:* Severe sepsis associated with refractory hypotension (BP<90/60) despite adequate fluid resuscitation and/or a serum lactate level >=4.0 mmol/L.

Sepsis Protocol

I. Recognition

- Sepsis is defined as at least two of the following signs and symptoms (SIRS) that are both present and new to the patient and suspicion of new infection

    - Hyperthermia >38.3°C or Hypothermia <36°C
    - Tachycardia >90 bpm
    - Leukocytosis (>12,000 µL-1) or Leukopenia (<4,000 µL-1) or >10% bands
    - Acutely Altered Mental Status
    - Tachypnea >20 bpm

- Severe sepsis includes SIRS and at least one of the following signs of hypoperfusion or organ dysfunction that is new and not explained by other known etiology of organ dysfunction

    - Hypotension (<90/60 or MAP <65)
    - Areas of mottled skin or capillary refill
    - Lactate > 2 mMol/L
    - Creatinine > 2 mg/dl

>3 seconds

- Disseminated intravascular coagulation (DIC)
- Acute renal failure or urine output<0.5 ml/kg/hr for at least 2 hours
- Cardiac dysfunction
- Platelet count <100,000
- Hepatic dysfunction as evidenced by Bilirubin >2 or INR >1.5
- Acute lung injury or ARDS

- New septic shock is defined as severe sepsis associated with refractory hypotension (BP<90/60) despite adequate fluid resuscitation and/or a serum lactate level ≥ 4.0 mmol/L
- Screening: Patients are screened for severe sepsis upon admission and daily thereafter using paper screening sheet (see below)

II. Resuscitation

Septic Shock Resuscitation Bundle

A. To be completed within 3-Hours

1. Measure Lactate level
2. Obtain blood culture prior to administration of antibiotic
3. Early and appropriate broad-spectrum antibiotic administration Timely re-evaluation of antibiotic therapy based on causative agent and susceptibilities is recommended
4. Administer 30 mL/kg crystalloid for hypotensive or lactate ≥ 4 mmol/L

B. To be completed within 6 hours

1. Apply vasopressors for hypotensive that does not respond to initial fluid resuscitation to maintain mean arterial pressure ≥ 65 mmHg
2. In the event of persistent arterial hypotension despite volume resuscitation or initial lactate ≥ 4 mmol/L (36 mg/dL)
    a. Maintain adequate central venous pressure (Target > 8 mmHg)
    b. Maintain adequate central venous saturation (Target > 70%)

Fluid responsiveness can be measured by dynamic parameters

- In patients who require large volume of resuscitation, dynamic hemodynamic monitor can be used

- Dynamic parameters are pulse pressure variation (PPV), stroke volume variation (SVV), and inferior vena cava (IVC) distensibility index.
    - Mechanically ventilated patients:
        - PPV (PPmax-PPmin)/(PPmean)>13% indicates fluid responsiveness and more fluid can be given
            - To measure PPV the Tidal volume should be ≥ 8 mL/Kg and no significant dysrhythmias exist
        - IVC distensibility index (max-min)/min value) > 18%.

    - Spontaneous breathing patients
        - Utilize passive leg raising test (PLR) together with measuring SV by Doppler or VTI by transthoracic echo TTE. Increase these indices by 15% or more indicate fluid responsiveness. See figure 2

Vasopressors

- The vasopressor of choice is noradrenaline
    - Dose 0.02-0.7 µg/kg/min
- IV dopamine or adrenaline can be added if blood pressure is poorly responsive to noradrenaline
    - Dopamine dose 10-20 µg/kg/min
    - Adrenaline dose 0.01-0.2 µg/kg/min
    - Caution: Adrenaline may worsen acidosis and increase the lactate
      Dopamine may cause serious cardiac dysrhythmia and should be used in patient with low risk of dysrhythmia
- Consider adding IV hydrocortisone 50 mg every 6 hours in refractory shock (norepinephrine dose exceeding 0.2 µg/kg/min)

Sepsis screening tools

Evaluation for severe sepsis screening tool

1. Is the patient's history suggestive of a New infection?

○ Pneumonia, Empyema	○ Soft tissue infection	○ Endocarditis
○ Urinary tract infection	○ Bone, joint infection	○ Implantable device infection
○ Acute abdominal infection	○ Wound infection	
○ Meningitis	○ Blood stream catheter infection	○ Others

○ Yes ○ No

2. Are any two of the following signs and symptoms of infections both present and new to the patients?

○ Hyperthermia > 38 ^{o}C	○ Acute altered mental status
○ Hypothermia < 36 ^{o}C	○ Leukocytosis (WBC > 12.000)
○ Tachycardia > 90 bpm	○ Leukopenia (WBC < 4.000)
○ Tachypnea > 20 bpm	○ Hyperglycemia (Blood glucose >120 mg/dl) in absence of diabetes

○ Yes ○ No

If the answer is yes to both questions 1 and 2 suspicious of infection is present

- Obtain: Blood lactate, Blood culture, CBC with differential, and basic chemistry lab including bilirubin
- At the physician discretion obtain: chest x-ray, CRP, CT scan, amylase, lipase

3. Are any of the following organ dysfunction criteria present at the site remote from the site of infection that are not considered to be chronic condition?
   - ○ SBP < 90 mmHg or MAP < 65 mmHg
   - ○ SBP decrease > 40 mmHg from baseline
   - ○ Bilateral pulmonary infiltrate with a new oxygen requirement to maintain SPO2 > 90%
   - ○ Creatinine > 2 mg/dl or urine output < 0.5 ml/kg/hour for > 2 hours
   - ○ Bilirubin > 2 mg/dl
   - ○ Platelet count < 100.000
   - ○ Coagulopathy (INR> 1.5)
   - ○ Lactate > 2 mmol/L (18 mg/dl)

If the suspicion of infection is present AND organ dysfunction is present, the patient meets the criteria for **SEVERE SEPSIS** and should be entered into severe sepsis protocol.

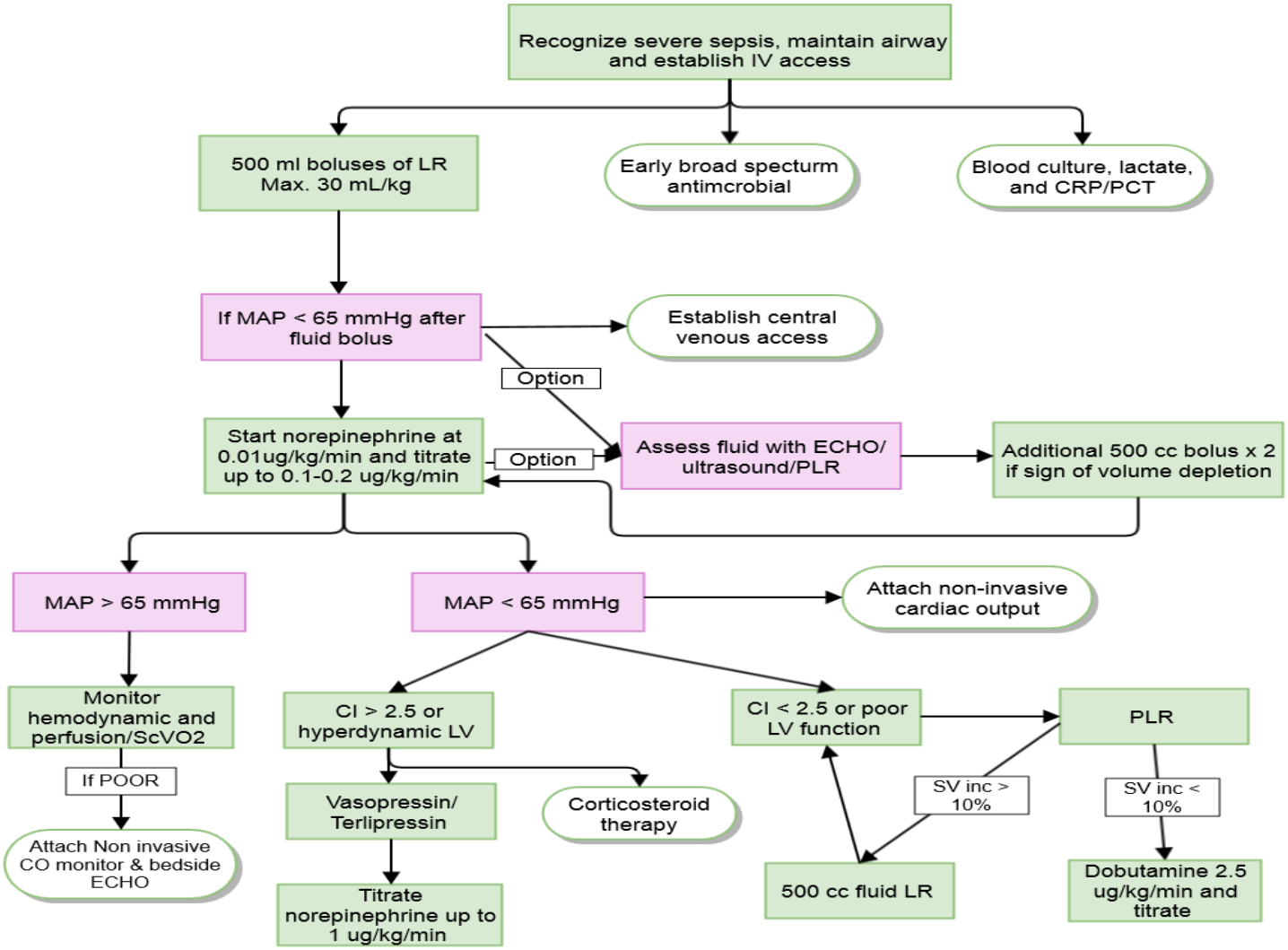

Figure 8: Severe sepsis and septic shock Resuscitation Algorithm [3]

References

2. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM, Nunnally ME, Townsend SR, Reinhart K, Kleinpell RM, Angus DC, Deutschman CS, Machado FR, Rubenfeld GD, Webb SA, Beale RJ, Vincent JL, Moreno R; Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41:580-637.
3. Seif D, Perera P, Mailhot T**.** Bedside ultrasound in resuscitation and therapid ultrasound in shock protocol. Crit Care Res Pract.2012;2012:503254.
4. Marik PE. Early management of severe sepsis: concepts and controversies. Chest. 2014;145:1407-18.

Fever Assessment

Basic principle

- The Society of Critical Care Medicine and the Infectious Disease Society of America considers a temperature of 38.3◦C or greater as a fever in an ICU patient which warrants further evaluation.
- This does not necessarily imply that a temperature below 38.3◦C does
- The onset of fever in the intensive care unit patient must be approached systematically and guided by clinical findings.

Infectious causes of fever

- Ventilator associated pneumonia
- Catheter-related bloodstream infection (CRBI)
- Primary septicemia
- Sinusitis
- Surgical site/wound infection
- Clostridium difficile colitis
- Cellulitis/infected decubitus ulcer
- Urinary tract infection (urosepsis)
- Suppurative thrombophlebitis
- Endocarditis
- Diverticulitis
- Septic arthritis
- Abscess/empyema

Non-Infectious causes of fever

- Drug fever
    - b -Lactam, antiepileptics, sulfonamides
    - Antipsychotics (neuroleptic malignant syndrome, serotonin syndrome)
- Blood products, IV contrast, immunoglobulins, albumin
- CNS causes: blood in cerebrospinal fl uid, pontine bleed
- Pulmonary/cardiac causes: acute respiratory distress syndrome, pulmonary emboli, fat emboli, pericarditis
- Abdominal causes: ischemic gut, pancreatitis, acalculous cholecystitis
- Metabolic: adrenal insufficiency, thyroid storm, gout
- Postoperative fever (48 h), postprocedure (bronchoscopy)
- Thrombophlebitis, decubitus ulcer, hematoma, deep venous thrombosis (DVT)

Evaluation of new fever in ICU (See algorithm below)

- Blood cultures are recommenced in all ICU patients who develop a fever.
- If catheter-related sepsis is suspected, two peripheral blood cultures should be obtained with an additional culture from each indwelling catheter.
- Expressed purulence from an intravascular catheter insertion site should be cultured.
- Do not routinely culture removed intravascular catheters. Culture only those suspected of being the source of infection.
- If a lower respiratory tract infection is suspected, obtain a portable AP chest radiograph.
- Quantitative cultures obtained by either bronchoscopy or catheter lavage should be obtained if pneumonia is suspected.
- Pleural fluid should be cultured if an adjacent infiltrate is noted or infection is suspected.
- In patients whose clinical picture is consistent with infection and in whom no clinically obvious source has been documented
    - Removal of all central lines greater than 48 h old
    - Evaluation for C. difficile infection should begin with a C. difficile toxin EIA.
    - CT scan of the sinuses with removal of all nasal tubes
- Send stool cultures for enteric pathogens or ova and parasite only if diarrhea was present prior to ICU admission, the patient is immunocompromised or it is epidemiologically indicated.
- Obtain urine for microscopic exam, Gram stain and culture in all high risk patients showing signs or symptoms of UTI.
- If the patient is at risk of abdominal sepsis or has any abdominal signs (tenderness, distension, unable to tolerate enteral feeds), CT scan of abdomen is indicated. Patients with right upper quadrant tenderness require an abdominal ultrasound or CT examination.
- Surgical wounds with suspected infection should be opened to obtain samples for Gram stain and culture. Cultures of the skin overlying a wound should not be performed.
- If CNS infection is suspected, send CSF for Gram stain and culture, glucose, protein, and cell count with differential.
- Chest radiographs, urinalysis, or urine cultures are NOT indicated in the first 72 hours post-operatively unless history and clinical findings suggest a high probability of infection.
- Noninfectious causes of fever should be investigated, including new medications and administration of blood products.
- If fever is accompanied by altered consciousness or focal neurologic deficits, lumbar puncture or evaluation of CSF from an indwelling ventriculostomy should be considered.

- All neutropenic patients with fever and patients with severe or progressive signs of sepsis should be started on broad-spectrum anti-microbial therapy immediately after obtaining appropriate cultures.

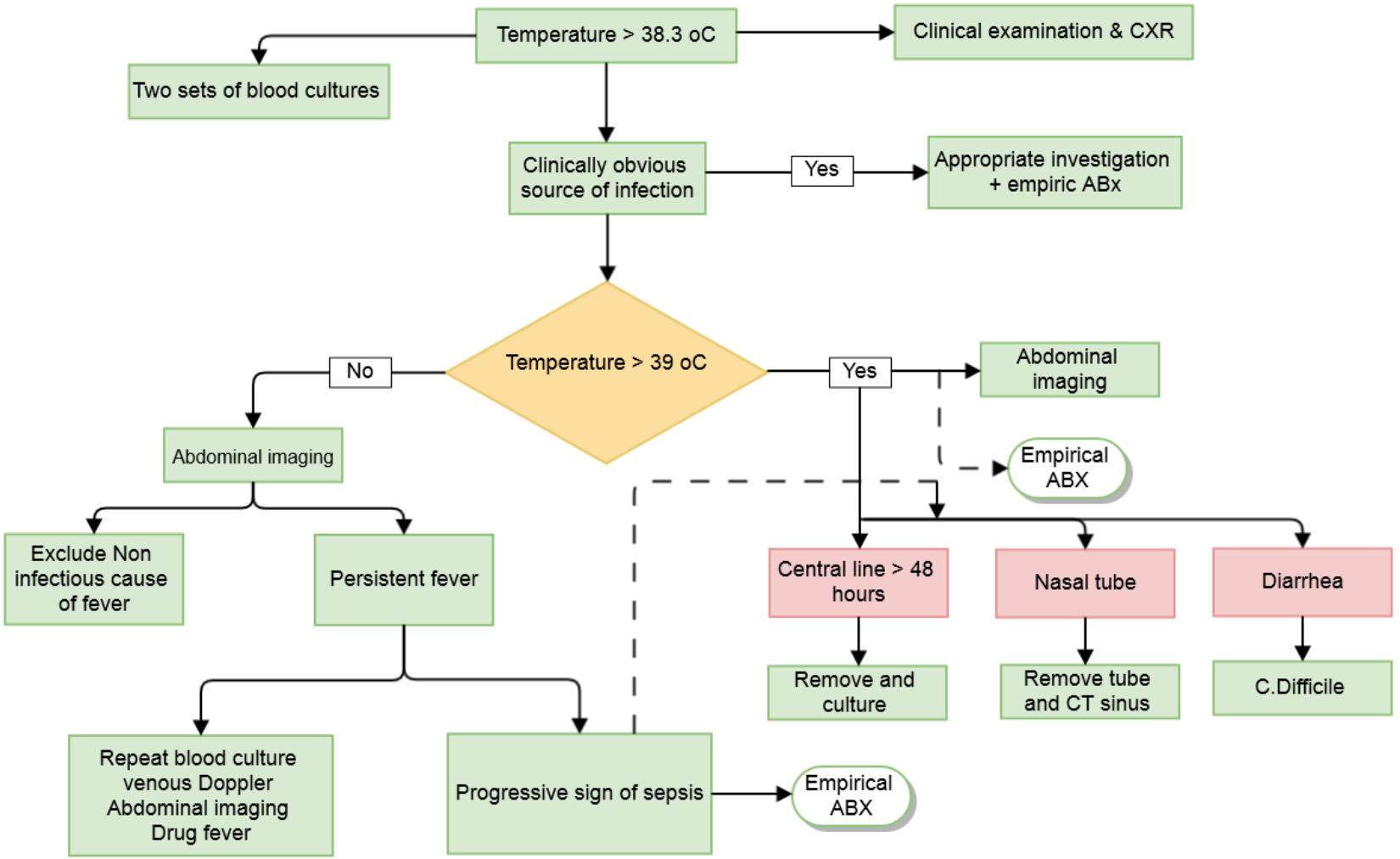

Figure 9: Fever Management Protocol [2]

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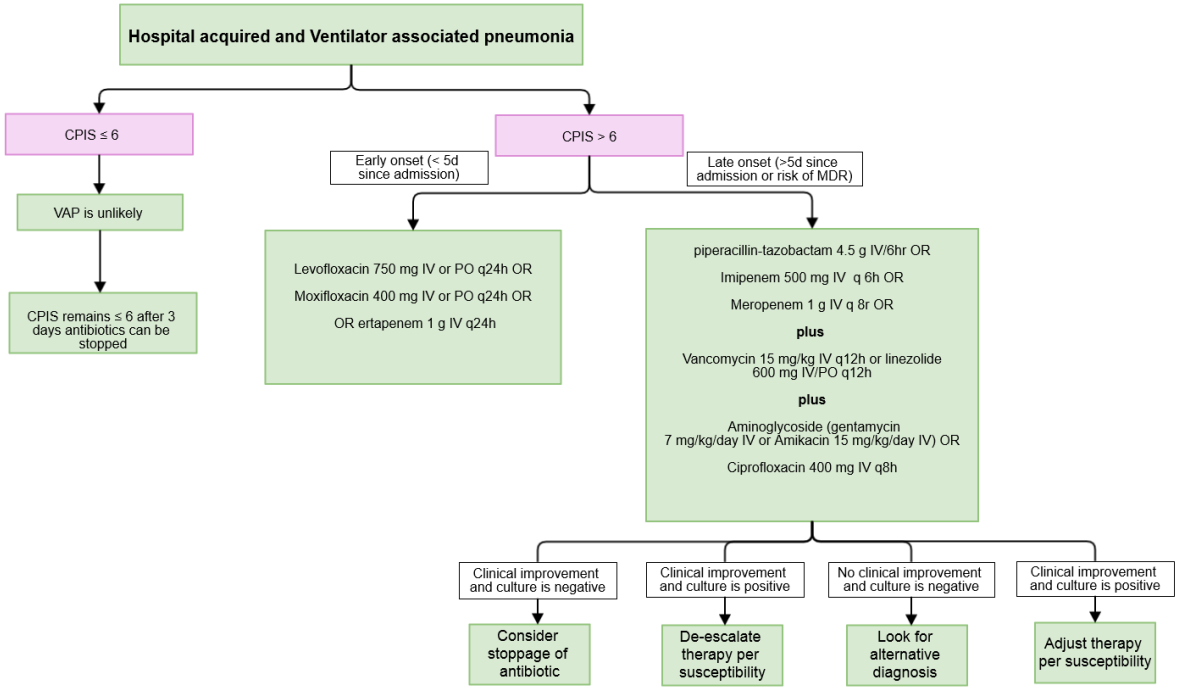
2. Claridge JA et al. The "fever workup" and respiratory culture practice in critically ill trauma patients. J Crit Care 2010; 25:493-500.

Nosocomial Infection

Hospital acquired and Ventilator Associated Pneumonia



- **Diagnosis**
  - Bacteria in endotracheal suction may represent tracheal colonization and NOT infection.
  - Tracheal colonization of Gram-negatives and S. aureus is not eradicated even though lower airways are sterilized. Thus, post-treatment cultures in the absence of clinical deterioration (fever, rising WBC, new infiltrates, worsening ventilatory status) are not recommended.
- **Definitive therapy**
  - De-escalate antimicrobial based on sensitivities
  - Consider Linezolid for documented MRSA pneumonia
  - Consider combination therapy for Pseudomonas for the first 5 days of therapy.
  - Inhaled Colistin can be used as adjunctive therapy in pseudomonas and acinetobacter
- **Duration of therapy**
  - Three days if CPIS remains ≤ 6 in patients with initial CPIS ≤ 6; VAP is unlikely
  - Eight days if the patient has clinical improvement except for Pseudomonas in which 15 days is recommended
  - Consider extended therapy (15 days) if CPIS > 6 at Day 8

Figure 10: Ventilator Associated Pneumonia

Table 1: Modified Clinical pulmonary infection score

CPIS point	0	1	2
Tracheal secretions	Rare	Abundant	Purulent
Leukocytic count	> 4000 and < 11000	< 4000 and >11000	< 4000 and >11000 + band form
Temperature	> 36.5 and < 38.4	> 38.5 and < 38.9	> 39 or < 36
PaO2/FIO2	> 240 or ARDS		≤ 240 and no ARDS
Chest X-ray	No infiltrate	Diffuse infiltrate	Localize infiltrate
Culture of tracheal aspirate	Negative		Positive

Community Acquired Pneumonia

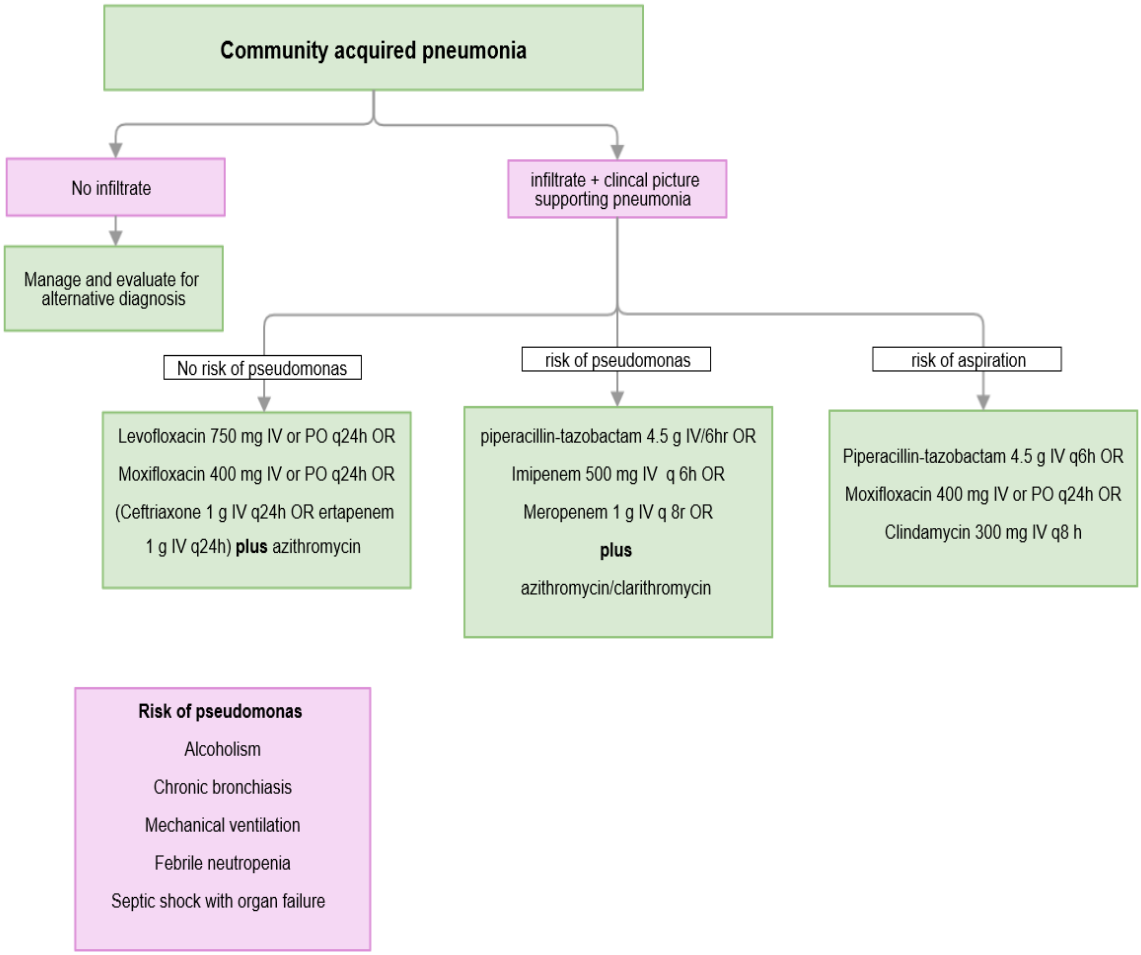


Figure 11: Management of community acquired pneumonia

Community Acquired abdominal infection

Figure 12: Management of Community Acquired abdominal infection

Health Care Associated abdominal infection

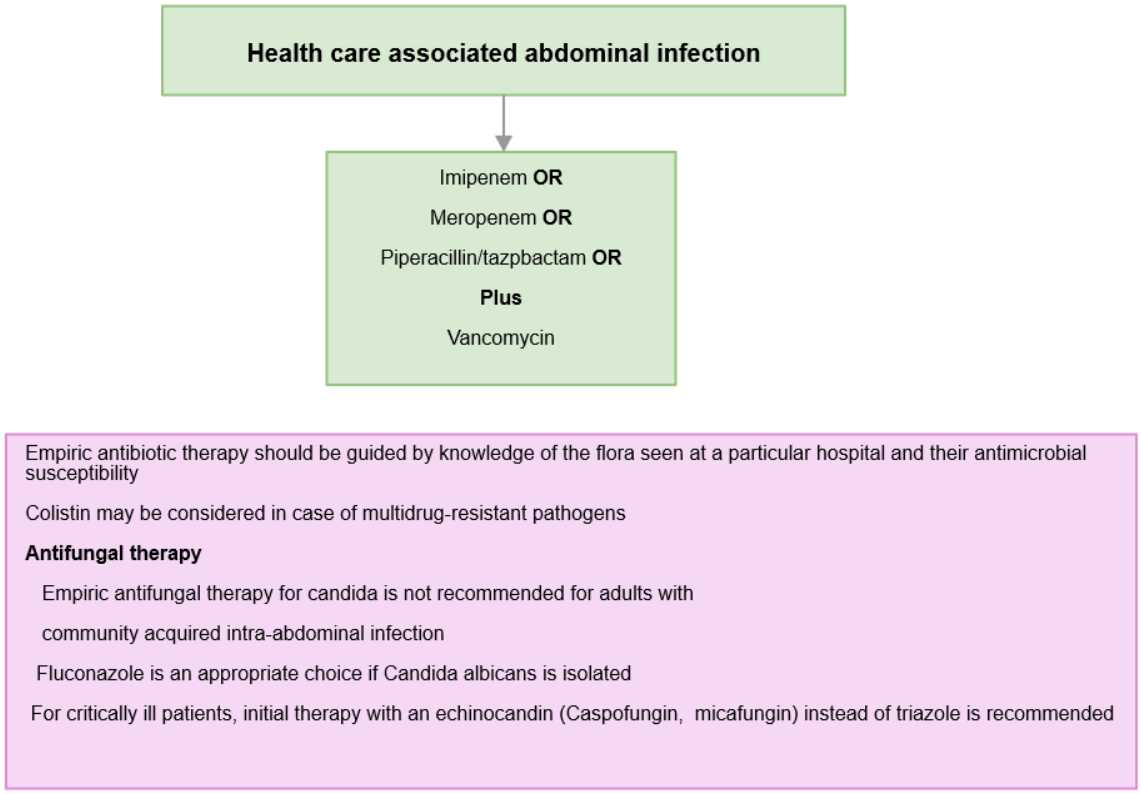


Figure 13: Management of Health Care Associated abdominal infection

Table: Initial Intravenous Adult Dosages of Antibiotics for Empiric Treatment of Complicated Intraabdominal Infection	
Antibiotic	**Adult Dose**
B lactam/b-lactamase inhibitor combination	
• **Piperacillin tazobactam**	4.5 g every 6 h
Carbapenems	
• **Ertapenem**	1 g every 24 h
• **Imipenem/cilistatin**	500 mg every 6 h or 1 g every 8 h
• **Meropenem**	1 g every 8 h
Cephalosporins	
• **Cefazolin**	1–2 g every 8 h
• **Cefepime**	2 g every 8–12 h
• **Cefotaxime**	1–2 g every 6–8 h
• **Cefoxitin**	2 g every 6 h
• **Ceftazidime**	2 g every 8 h
• **Ceftriaxone**	1–2 g every 12–24 h
• **Cefuroxime**	1.5 g every 8 h
Tigecycline	100 mg initial dose, then 50 mg every 12 h
Fluoroquinolones	
• **Ciprofloxacin**	400 mg every 12 h
• **Levofloxacin**	750 mg every 24 h
Metronidazole	500 mg every 8–12 h or 1500 mg every 24 h
Aminoglycosides	
• **Gentamicin or tobramycin**	5–7 mg/kg every 24 h
• **Amikacin**	15–20mg/kg every 24 h (initial dose should be based on adjusted body weight)
Aztreonam	1–2g every 6–8h
Vancomycin	15–20 mg/kg every 8–12 h (initial dose should be based on total body weight)

Catheter related blood stream infection (CLBSI)

Bloodstream infection related to a short-term central venous catheter (CVC) is defined as bacteremia or fungemia in a patient with the CVC in place

- Prevention of CLBSI
    - Use aseptic technique including the use of a cap, mask, sterile gown, sterile gloves, and a large sterile sheet, for the insertion of CVCs
    - Wear clean or sterile gloves when changing the dressing on intravascular catheters.
    - Disinfect clean skin with an appropriate antiseptic before catheter insertion and during dressing changes. 70% alcohol can be used
    - Do not use topical antibiotic ointment or creams on insertion sites
    - Do not routinely replace central venous solely for the purposes of reducing the incidence of infection
    - When adherence to aseptic technique cannot be ensured (i.e., when catheters are inserted during a medical emergency), replace all catheters as soon as possible and after no longer than 48 hours
    - Replace any short-term CVC if purulence is observed at the insertion site, which indicates Infection
    - Replace catheter-site dressing if the dressing becomes damp, loosened, or visibly soiled
    - Replace dressings used on short-term CVC sites every 2 days for gauze dressings and at least every 7 days for transparent dressings,
    - Clean injection ports with 70% alcohol or an iodophor before accessing the system
    - Cap all stopcocks when not in use
    - Minimize contamination risk by wiping the access port with an appropriate antiseptic and accessing the port only with sterile devices
    - Complete the infusion of lipid-containing solutions (e.g., 3-in-1 solutions) within 24 hours
    - Complete infusions of blood or other blood products within 4 hours of hanging the blood
    - Do not use hemodialysis catheters for blood drawing or applications other than hemodialysis except during dialysis or under emergency circumstances.
- Diagnosis of CLBSI: at least one of the following diagnostic criteria should be met:
    - Cultures of the catheter tip and of the peripheral blood grow the same organism.
        - Catheter tip culture should be quantitative, with more than 10^2 colony-forming units (cfu) per catheter segment, or semiquantitative, with more than 15 cfu per catheter segment.
    - Blood drawn from the catheter lumen grows the same organism as blood drawn from a peripheral vein.

- Initial management of suspected blood-stream infection related to short-term central venous catheters

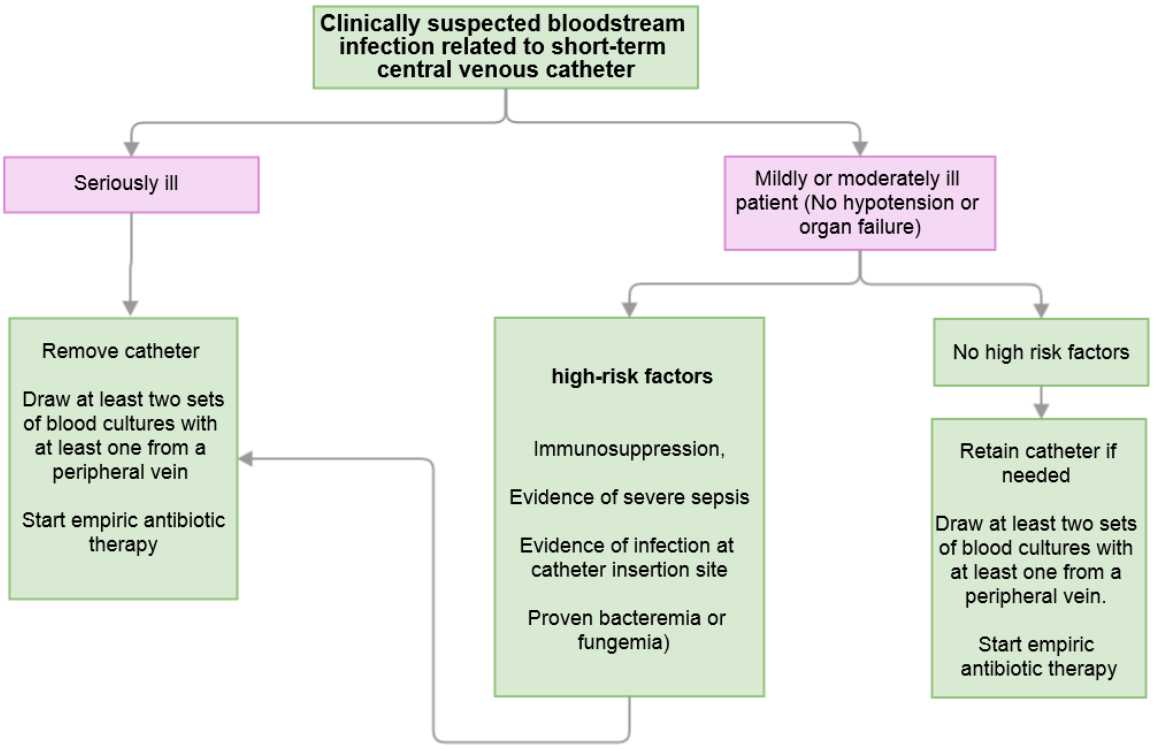


Figure 14: Management of clinically suspected blood stream infection related to short term CVL

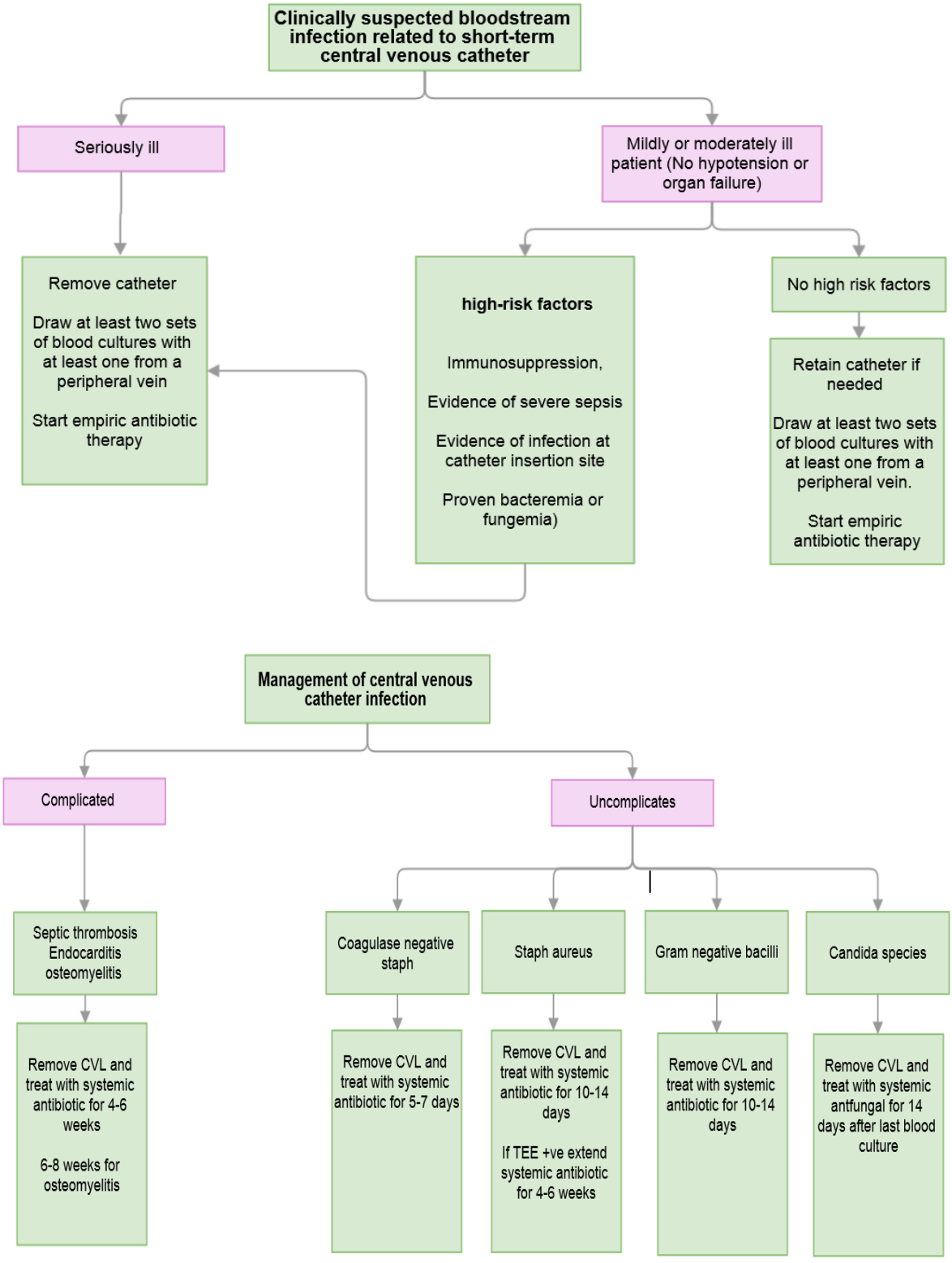


Figure 15: Management of CLBSI

Invasive candidiasis in ICU

- Prevention of C/IC in intensive care unit patients
    - Routine antifungal prophylaxis of all intensive care unit (ICU) patients is not recommended.
    - High-risk subgroups of patients who may be candidates for prophylaxis include the following:
        - ICU patients with recurrent gastrointestinal perforation or anastomotic leakage. In this selected high-risk group, IV fluconazole 400 once daily may be administered.
        - There are insufficient data to support specific recommendations for antifungal prophylaxis in severe acute pancreatitis
- Yeast in a blood culture SHOULD NOT BE considered a contaminant
- Treatment
    - Immunocompromised (transplant, neutropenic, AIDS)
        - Start amphotericin B and wait for identification
    - Non-Immunocompromised
        - Patients who are clinically stable and have not received prior long-term azole therapy→ Fluconazole 800 mg IV/PO X 1 dose, then 400 mg IV/PO once daily
        - Patients who are NOT clinically stable due to Candidemia or have received prior long-term azole therapy→ Echinocandins (See algorithm below)
- Non-pharmacologic management
    - Removal of all existing central venous catheters is highly recommended.
    - Patients should have blood cultures daily or every other day until candidemia is cleared.
    - Patients should have an ophthalmologic examination to exclude candidal endophthalmitis prior to discharge, preferably once the candidemia is controlled.
    - Echocardiography can be considered if the patient has persistent candidemia on appropriate therapy.
- Endophthalmitis
    - Management in conjunction with Ophthalmology
    - Due to poor CNS and vitreal penetration, treatment with echinocandins is NOT recommended.
    - Preferred therapy

- Amphotericin B 1 mg/kg IV once daily OR AmBisome (liposomal amphotericin) 5 mg/kg IV once daily

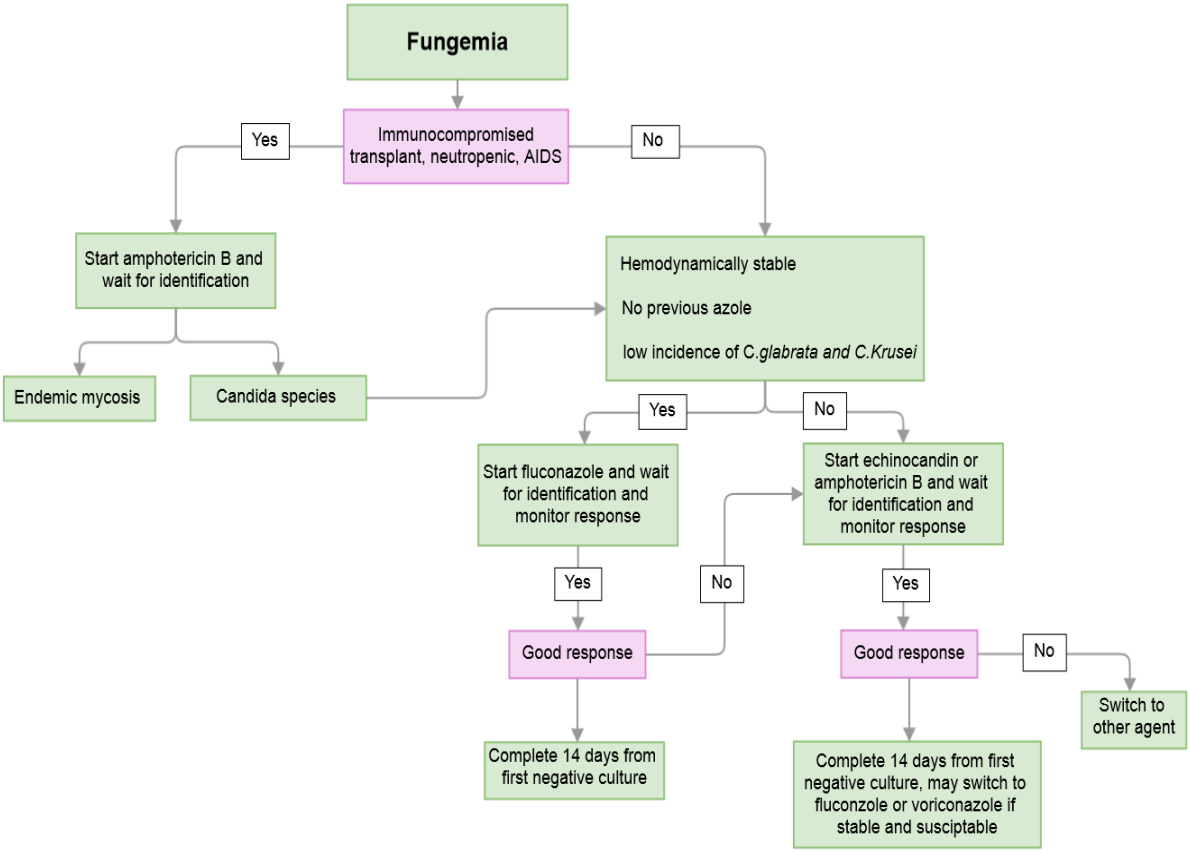


Figure 16: Management of fungemia

Table 2: IDSA guidelines of treating invasive fungal infectionle 1:.....

Summary of IDSA Guidelines for Treating Invasive Candidiasis and Aspergillosis

Disease State	First-Line Treatment	Alternative Regimen(s)
Invasive aspergillosis	Voriconazole 6 mg/kg IV q12h for 2 doses; then 4 mg/kg IV q12h or 200 mg PO q12h	Lipid amphotericin B 3–5 mg/kg IV q24h Caspofungin 70-mg IV loading dose; then 50 mg/day IV Micafungin 100–150 mg/day IV Posaconazole 800 mg/day PO in 2–4 divided doses Itraconazole dose depends on formulation
Candidemia (non-neutropenic patient; moderate-severe illness)	Caspofungin 70-mg IV loading dose; then 50 mg/day IV Micafungin 100 mg/day IV Anidulafungin 200-mg IV loading dose; then 100 mg/day IV	Fluconazole 800-mg IV loading dose; then 400 mg/day IV or PO
Candidemia (neutropenic patient)	Caspofungin 70-mg IV loading dose; then 50 mg/day IV Micafungin 100-mg IV daily Anidulafungin 200-mg IV loading dose; then 100 mg/day IV	Fluconazole 800-mg IV loading dose; then 400 mg/day IV/PO Voriconazole, if mold coverage desired Voriconazole 6 mg/kg IV q12h for 2 doses; then 4 mg/kg IV q12h or 200 mg PO q12h
Candida glabrata	Echinocandin (see above)	Fluconazole or voriconazole with susceptibility testing
Candida parapsilosis	Fluconazole	Echinocandin, if already responding to therapy
Solid-organ transplant recipient (prophylaxis)	Fluconazole 200–400 mg/day IV/ PO for 7–14 days	Liposomal amphotericin B 1–2 mg/kg/day IV for 7–14 days
ICU prophylaxis (high-risk patients only)	Fluconazole 400 mg/day IV/PO	

ICU = intensive care unit; IDSA = Infectious Diseases Society of America; IV = intravenous; PO = by mouth; q12h = every 12 hours; q24h = every 24 hours.

Specific Types of infections

Deep tissue infection (Necrotizing fasciitis)

- These are SURGICAL EMERGENCIES! antibiotics are only an adjunct to prompt debridement EMPIRIC TREATMENT (adjunct to surgery)
    - Vancomycin (see dosing section, p. 145) PLUS [Piperacillin/tazobactam 3.375 g IV Q6H OR Cefepime 1 g IV Q8H] PLUS Clindamycin 600-900 mg IV Q8H
    - In penicillin allergy: Vancomycin (see dosing section, p. 145) PLUS [Ciprofloxacin 400 mg IV Q8H PLUS Clindamycin 600-900 mg IV Q8H

Meningitis – Empiric treatment

- Antibiotics should be started as soon as the possibility of bacterial meningitis becomes evident, ideally within 30 minutes.
- Do not wait for CT scan or lumbar puncture results. If lumbar puncture must be delayed, get blood culture and start therapy.

Host	Preferred antibiotics	Alternative therapy
Immuno competent* age < 50	Vancomycin PLUS Ceftriaxone	Chloramphenicol PLUS Vancomycin
Immunocompetent* age > 50	Vancomycin PLUS Ceftriaxone PLUS Ampicillin	Chloramphenicol PLUS Vancomycin PLUS TMP/SMX
Immuno -compromised	Vancomycin PLUS Ceftriaxone PLUS Ampicillin	Vancomycin PLUS TMP/SMX PLUS Ciprofloxacin
Post neurosurgery or penetrating head trauma	Vancomycin PLUS Cefepime	Vancomycin PLUS Ciprofloxacin
Infected shunt	Vancomycin PLUS Cefepime	Vancomycin PLUS Ciprofloxacin

- Immunocompromised is defined as HIV infection or AIDS, receiving immunosuppressive therapy, or after transplantation.
- Addition of dexamethasone is recommended in all adult patients with suspected pneumococcal meningitis.
    - Dose: 0.15 mg/kg IV Q6H for 2–4 days
    - The first dose must be administered 10–20 minutes before or concomitant with the first dose of antibiotics.
    - Dexamethasone should not be given to patients who have already started antibiotics.

- Continue dexamethasone only if the CSF Gram stain shows Gram-positive diplococci or if blood or CSF grows S. pneumoniae

CNS shunt infection

- Diagnosis:
  - Culture of cerebrospinal fluid remains the mainstay of diagnosis.
  - Clinical symptoms may be mild and/or non-specific, and CSF chemistries and leukocyte counts may be normal.
- Empiric Therapy:
  - Vancomycin**:** (see dosing section, p. 145) PLUS Cefepime 2 g IV Q8H OR
  - Penicillin Allergy: Vancomycin PLUS Ciprofloxacin 400 mg IV Q8H
- Removal of all components of the infected shunt with external ventricular drainage or intermittent ventricular taps in combination with the appropriate intravenous antibiotic therapy leads to the highest effective cure rates
- The role of intraventricular antibiotics is controversial, and generally limited to refractory cases or cases in which shunt removal is not possible.
- Intraventricular antibiotics
  - Amikacin: 30 mg Q24H
  - Gentamicin: 5 mg Q24H
  - Tobramycin: 5 mg Q24H
  - Vancomycin: 20 mg Q24H

Diabetic foot infections

Treatment depends on clinical severity

- Moderate severity: > 2 cm of cellulitis, spread beneath the superficial fascia, deep tissue abscess, gangrene, involvement of muscle, tendon, joint, or bone
  - Ertapenem 1 g Q24H OR
  - Ciprofloxacin* 400 mg IV Q12H PLUS ONE of the following
  - [Clindamycin 600 mg IV Q8H/300 mg PO TID OR Metronidazole 500 mg IV/PO TID] BUT avoid fluoroquinolones in patients who were on them as outpatients
  - If patient at risk for MRSA, add Vancomycin to regimens that do not include Clindamycin.
  - Risk factors for MRSA
    - History of colonization or infection with MRSA
    - Recent (within 3 months) or current prolonged hospitalization > 2 weeks
- Severe infection: As moderate severity PLUS systemic toxicity or metabolic instability
  - Pipercillin/tazobactam 4.5 g IV Q6H OR
  - Carpabenems OR

- Ciprofloxacin* 400 mg IV Q8H PLUS Clindamycin 600 mg IV Q8H
- Avoid fluoroquinolones in patients who were on them as outpatients.
- If patient at risk for MRSA
  - Carpabenems OR Piperacillin/tazobactam 4.5 g IV Q6H PLUS Vancomycin OR
  - Ciprofloxacin* 400 mg IV Q8H PLUS Metronidazole 500 mg IV Q8H PLUS Vancomycin

Infective Endocarditis

Duke criteria for infective endocarditis

- Definite endocarditis
  - Presence of 2 major criteria OR 1 major AND 3 minor OR 5 minor Possible endocarditis
- Possible endocarditits
  - Presence of 1 major AND 1 minor OR 3 minor criteria
- Major criteria
  - Microbiologic
    - Two separate blood cultures positive for a typical organism: viridans streptococci, S. bovis, HACEK, S. aureus, Enterococcus spp.
    - Persistent bacteremia with any organism as evidenced by: 2 positive blood cultures drawn at least 12 hours apart OR 3/3 positive blood cultures with at least 1 hour between the first and last OR the majority of more than 4 cultures positive from any time period.
    - Positive Coxiella burnetti (Q fever) culture or serology.
  - Echocardiographic (TEE strongly recommended for prosthetic valve)
    - Vegetation (on valve or supporting structure OR in path of regurgitant jet)
    - Abscess
    - New dehiscence of prosthetic valve
  - Physical exam
    - regurgitant murmur (worsening of old murmur is NOT sufficient)
- Minor criteria
  - Predisposing condition: previous endocarditis, injection drug use, prosthetic valve, ventricular septal defect, coarctation of the aorta, calcified valve, patent ductus, mitral valve prolapse with regurgitation, IHSS or other valvular heart disease
  - Fever ≥ 38.0°C (100.4°F)
  - Embolic events: arterial or pulmonary emboli, conjunctival hemorrhage, retinal hemorrhage, splinter hemorrhage, intracranial hemorrhage, mycotic aneurysm

- Immunologic phenomenon: Osler nodes, glomerulonephritis, positive rheumatoid factor
- Positive blood cultures that don't meet criteria above OR serologic evidence of active infection with an organism known to cause endocarditis BUT single positive cultures for coagulase-negative staphylococci are NOT considered even a minor criterion

Management

A. Native valve endocarditis
    - Vancomycin PLUS Gentamicin 1 mg/kg IV Q8H
B. Prosthetic valve endocarditis
    - Vancomycin PLUS Gentamicin 1 mg/kg IV Q8H
      AND
    - Rifampin 300 mg PO Q8H after blood cultures have cleared

Table 3: Vancomycin dosing and monitoring

Weight (kg)	CrCl (mL/min) >60	30–59	15–29	<15 or dialysis, (HD,CVVHD)
40–49	750 mg Q12H	750 mg Q24H	750 mg Q48H	1000 mg, then redose by level†
50–59	1000 mg Q12H	1000 mg Q24H	1000 mg Q48H	1000 mg, then redose by level†
60–75	1000 mg Q12H	1000 mg Q24H	1000 mg Q48H	1000 mg, then redose by level†
76–90	1250 mg Q12H	1250 mg Q24H	1250 mg Q48H	1250 mg, then redose by level†
90–110	1500 mg Q12H	1500 mg Q24H	1500 mg Q48H	1500 mg, then redose by level†

†For patients with CrCl <15 mL/min and not receiving hemodialysis redose when random level <15–20 mcg/mL. For patients receiving maintenance hemodialysis, redose after hemodialysis session if pre-hemodialysis level <25 mcg/mL for pneumonia, osteomyelitis, endocarditis or bacteremia. For meningitis, consider redosing patient if pre-hemodialysis level <30 mcg/mL. Loading dose should not be used in these patients.

Multi-drug resistant gram negative bacteria (MDR-GNB)

General principles

- Multidrug resistance gram negative bacteria (MDR-GNB): is defined as is an isolate that is non-susceptible to at least one agent in at least three antimicrobial categories, which are potentially active against the respective GNB.
- Extensively drug resistance (XDR): is defined as isolate that is non-susceptible to at least one agent in all but two or fewer antimicrobial categories, which are potentially active against the respective GNB.
- Pandrug-resistance (PDR): is defined as isolate that is non-susceptible to all agents in all antimicrobial categories for this isolate

Management

- Combination therapy is the mainstay of treatment of XDR and PDR gram negative bacteria through
    - Maximizing bacterial killing
    - Minimizing emergence of resistance
    - Enable shorter therapy duration
    - Improve clinical and microbiological outcome
- An algorithm based on minimum inhibitory concentration (MIC) of commonly used antimicrobial agents is suggested to optimize the use of combination therapy [8]

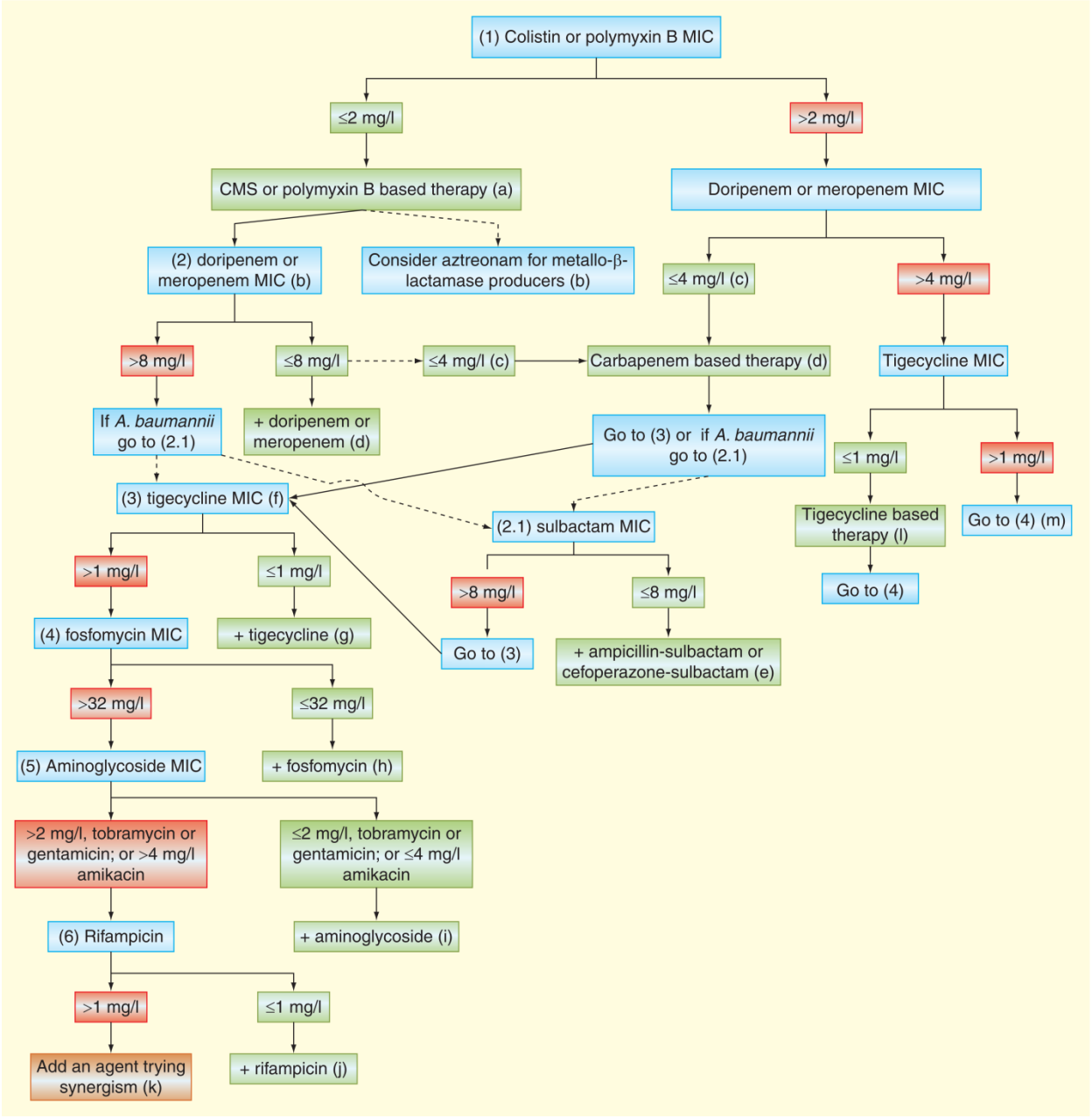


Figure 17: Flowchart for selecting mainstream and adjuvant therapy against Gram-negative bacteria [8]

a) Colistin methanesulfonate sodium (CMS) –

- Loading dose: 150,000 IU (corresponding to ~5 mg colistin base activity) weight in kg; caution should be taken in using any dose above the current maximum approved daily dose of 10 million IU (~300 mg of colistin base activity).
- Maintenance dose: started 12 or 24 h later: 9–12 million IU/day split into 2 or 3 doses (every 8 or 12 h) for patients with creatinine clearance ≥ 60 ml/min.
- Adjust for renal dysfunction

b) If the pathogen is suspected to be a metallo-b-lactamase-producing GNB, the aztreonam MIC may be evaluated at the same time as the MIC of the carbapenems.

c) Carbapenems

- Some authors suggest that if the MIC ≤ 4 mg/l for carbapenems, a carbapenem should be the cornerstone drug in the combination

d) Meropenem: 2 g every 8 h over 3–4 h. Imipenem may be used 1 g every 6 h, but there is few data concerning its stability in extended infusion and it poses a higher risk of convulsion at higher doses.

e) 9–12 g/day of the sulbactam component every 6–8 h infused over 3–4 h. High-dose extended infusion sulbactam may also be considered against organisms with MIC = 16 mg/l

f) If the organism is pseudomonas, we go directly to step 4

g) Tigecycline

- 200 mg as loading dose followed by 100 mg every 12 h for MIC = 0.5 or 1 mg/l, or 100 mg as loading dose followed by 50 mg every 12 h may be appropriate for MIC ≤ 0.25 mg.
- Higher doses may be considered for severe urinary tract infections
- If tigecycline is the cornerstone drug, high doses should always be considered regardless of the MIC.

h) Fosomycin

- high doses (20–24 g/day divided in 3 or 4 doses) are recommended for fosfomycin MIC = 16–32 mg/l. Lower doses (12–16 g/day) may be appropriate for MIC<16 mg/l.

i) Aminoglycosides

  - Gentamicin and tobramycin should be chosen on the basis of the lower MIC; MIC ≤ 0.5: 5 mg/kg once daily. MIC 1 or 2 mg/l: 7 mg/kg once daily (for MIC = 4 mg/l even higher doses may be more appropriate); a loading dose must be administered in critically ill patients.
  - Amikacin: 15 mg/kg once daily is more likely appropriate for MIC ≤4; for MIC = 8 or 16 mg/l higher doses may be necessary; a loading dose ‡25 mg/kg must be administered in critically ill patients.

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Mechanical Ventilation Protocol

Parameters for institution of ventilation

i) Clinical assessment is the most sensitive assessment of respiratory failure.
ii) Do not delay the initiation of ventilatory support pending results, blood gases or mechanical measurements where clinically indicated, e.g.
    - Threatened airway
    - Fatigue / exhaustion
    - Failure of secretion clearance
    - Overt respiratory failure
    - Speech impairment due to dyspnoea
    - Reduced GCS in the absence of other causes

Objective measurements are adjuncts to clinical assessment and must be used in the clinical context, e.g.

- PaO2/FIO_2 ratio remains the most convenient and widely used bedside index of gas exchange.
- In ventilated patient, oxygenation index (OI) incorporates the severity of oxygenation impairment (PaO_2/F IO_2 ratio) and mean airway pressure into a single variable:
    - OI = (FIO_2 X mPaw X 100)/PaO_2
    - OI > 30 is used to represent failure of conventional ventilation

Principles in optimizing ventilation in ICU patients

1. There is no evidence that a particular mode of mechanical ventilation is associated with survival benefit
2. Appropriate goal is far more important than chosing a particular mode of mechanicak ventilation
3. Low tidal volume ventilation should be instituted in all patients on mechanical ventilation. Target tidal volume of 6 mL/kg ideal body weight and plateau pressure of < 30 cmH2O
4. The optimal time to initiate ventilator rescue therapies is within 96 hours of onset of Acute Respiratory Distress Syndrome (ARDS)
5. The choice of rescue therapy should be based on equipment availability and clinician expertise. If the therapy does not result in improved oxygenation, it should be abandoned.

Low tidal volume Ventilation

- Calculate the ideal body weight of the patient
    - Male=50 + 0.91[height(cm)-152.4]kg
    - Female=45.5 + 0.91 [height(cm)-152.4]kg
- Mode: Pressure controlled ventilation (PCV) or volume controlled ventilation (VCV)
- Aim for tidal volume of 6 mL/kg IBW while not exceeding Pplat of 30 cmH2O. In PCV Pplat is equivalent to peak airway pressure. If VCV is used, Pplat needs to be measured regularly every 2-4 hr
- If Pplat > 30 cmH2O, decrease tidal volume by 1 mL/kg up to 4 mL/kg. If Pplat < 25 cmH2O tidal volume may be increased by 1mL/kg up to 8 mL/Kg if Pplat remains ≤ 25 cmH2O
- Adjust FIO2 and PEEP (cm H2O) to maintain PaO2 55–80 mm Hg.
    - Use PEEP 8-12 cmH2O if PaO2/FIO2 ≥ 250
    - Use PEEP > 12 cmH2O if PaO2/FIO2 < 250
- Keep the arterial PH > 7.1
    - pH <7.30, increase rate to maximum 35 breaths/min
    - pH <7.30 and rate = 35, consider bicarbonate administration
    - pH <7.15, consider increase in tidal volume by 1mL/kg even if Pplat > 30 cmH2O
    - Contraindication to permissive hypercapnia include intracranial hypertension, acute coronary syndrome, and right-sided failure with concomitant pulmonary hypertension

Strategies to improve severe hypoxemia

Definition of severe hypoxemia

- Oxygenation index > 30
- $PaO_2/F\ IO_2$ ratio ≤ 120

Ventilatory strategies

- The potential for lung recruitment can be identified by the use of a 30 minute trial of increase PEEP at 15 cmH2O. High potential are those at the end of the trial demonstrate all of the following
    - Increase SPO2 by 5%

    - Increase $PaO_2/F\ IO_2$ ratio
    - Increase in compliance
- Subsequent ventilator strategies is based on distinction between patients who are low potential recruiters (Non-recruiters) and high potential recruiters (recruiters)
- In non-recruiters no further recruitment manoeuvre should be used. Consider non-ventilatory strategies
- Steps of recruitment manoeuvre
    - Consider sedation and paralysis during manoeuvre.
    - Monitor for hypotension and desaturation.
    - Different types of recruitment manoeuvres can be performed
        - Sustained high inflation pressure
            - CPAP 30-50 cmH2O for 20-40 seconds
        - PCV with driving pressure 20-25 cmH2O with PEEP 20-25 cmH2O, RR 10/min, I:E 1:1, FIO_2 for 2 min.
        - PCV with stepwise increase in PEEP every 2 min, keeping the driving pressure constant up to PIP of 40-50 cmH2O (See the algorithm below)
    - At the end of recruitment manoeuvre perform ABG at FIO_2 1.0
        - PaO_2 +$PaCO_2$ ≥ 400 mmHg suggests that there is less than 5% of alveolar collapse.
        - PaO_2 +$PaCO_2$ < 400 consider repeating recruitment manoeuvre
    - Determine the optimal PEEP using the decremental PEEP technique.
        - Set PEEP at 20 cmH2O and reduce the PEEP in a stepwise fashion (1 cmH2O every 5 min) until decrement occurs as demonstrated by a decrease in PaO_2 (a reduction of more than 10% from the previous indicates the collapse pressure).
        - The optimal PEEP is set at 2 cmH2O above the collapse pressure.
        - Re-recruit the lung at the optimal PEEP level

Non-Ventilatory strategies

Prone positioning

- Indication of prone position in ARDS
    - Indicated in moderate to severe ARDS defined as PaO2/FIO2 < 150 on at least 5 cmH2O PEEP
- Steps of prone position
    - It should be instituted early in the course of disease within 24-48 hours of the onset of ARDS

    - Patients should be placed in a completely prone position for at least 16 consecutive hours.
    - The criteria for stopping prone treatment will be any of the following:
    - improvement in oxygenation (defined as a Pao2:Fio2 ratio of ≥150 mm Hg, with a PEEP of ≤10 cm of water and an Fio2 of ≤0.6
    - These criteria had to be met in the supine position at least 4 hours after the end of the last prone session).
- Contraindication to prone positioning
    - Absolute contraindications
        - spinal instability and unmonitored increased intracranial pressure.
    - Relative contraindications
        - open abdominal wounds,
        - multiple trauma with unstabilized fractures,
        - pregnancy,
        - severe hemodynamic instability
        - high dependency on airway and vascular access

Neuromuscular Blockers

- Indicated in moderate to severe ARDS defined as PaO2/FIO2 < 150
- It should be instituted early in the course of disease within 24-48 hours of the onset of ARDS
- Cisatracurium/ atracurium are the agents of choice

Moderate dose glucocorticoids

- Should be considered in patients with early ARDS (within 72 hours of diagnosis) with PaO2/FIO2 < 200
- The role of steroid in less severe cases PaO2/FIO2 > 200 is less clear
- The following regimen is as follow
    - 1 mg/kg/day D1 to D14
    - 0.5 mg/kg/day D15 to D21
    - 0.2 mg/kg/day D22 to D25
    - 0.125 mg/kg/day D26 to D28
- If extubated between D 1 –D14 proceed to D15 therapy
- Change to single oral dose when enteral feeding is restored

Other non-ventilatory strategies

- Conservative fluid management with or without frusemide may decrease days of mechanical ventilation. Hypovolemia should be avoided

- Avoid drug that inhibit pulmonary vasoconstriction such as nitrates, calcium channel blocker, dopamine
- Albumin 20% with Frusemide may be considered in patients who are hypoproteinemic
    - 25 g albumin IV over 1.5-2 hr q 8 hrs with continuous infusion of frusemide for 5 days.

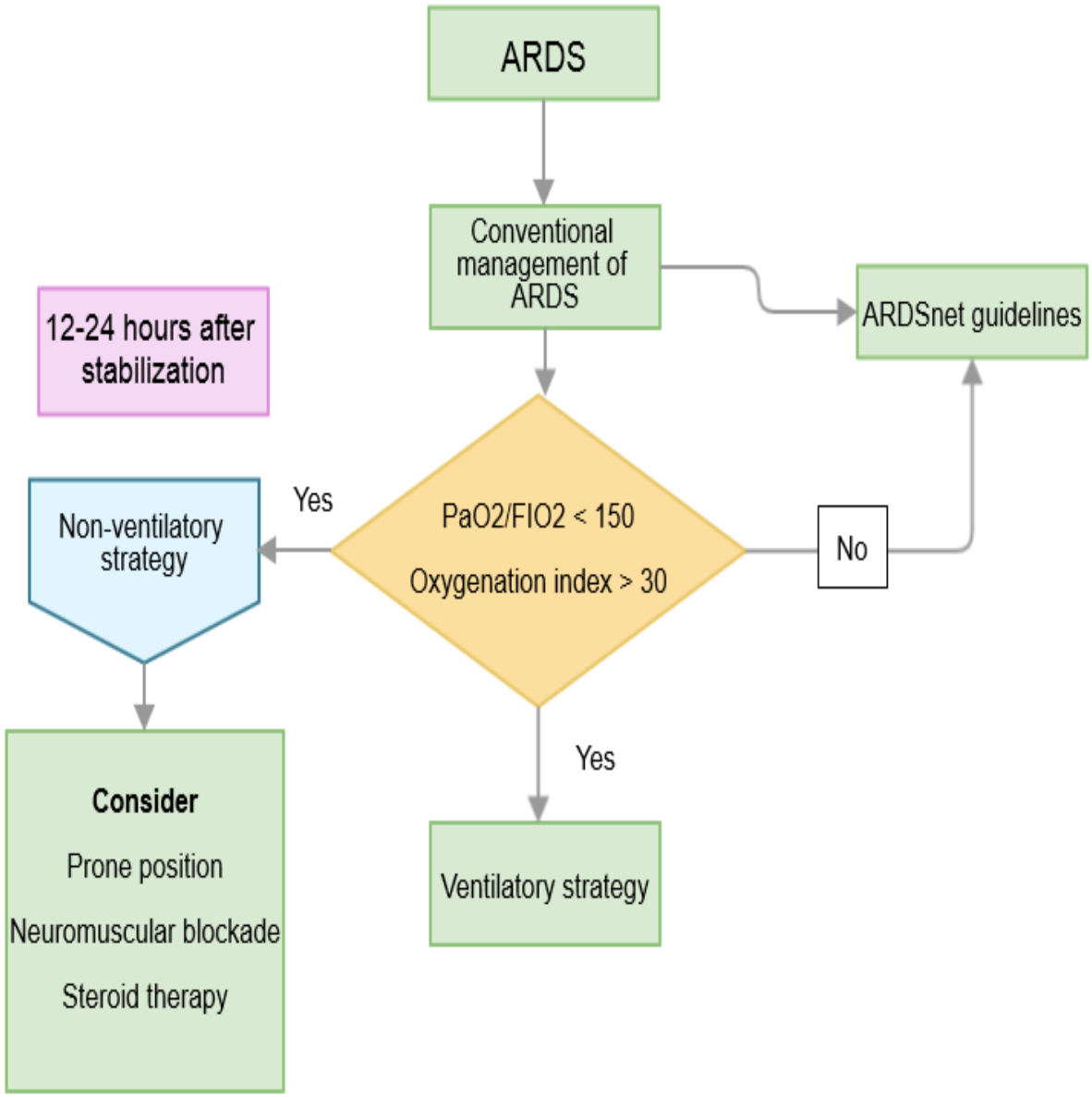

Figure 18: Algorithm of ARDS management protocol [1]

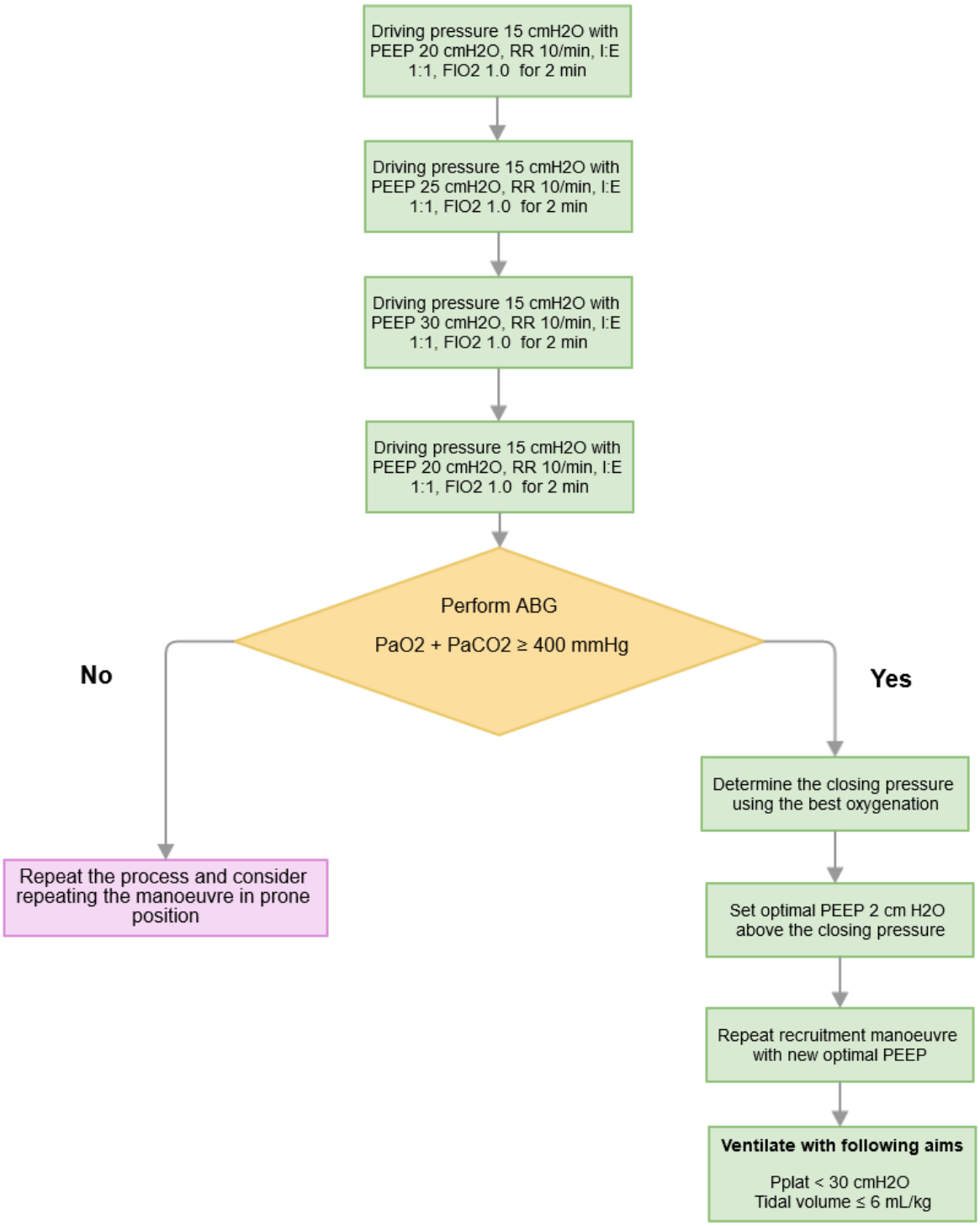

Figure 19: Stepwise approach of lung recruitment [4]

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Weaning of Mechanical ventilation

- Most patients require a period of rest after intubation, but consideration of weaning process should begin very soon after intubation.
- The cause of the patients' initial respiratory failure must be significantly improved or resolved before consideration of readiness to wean.
- Evaluation of readiness to wean should be started early and repeated and repeated at least on a daily basis.
- The patient must be awake, cooperative hemodyamically stable and able to cough and protect airway before extubation.

Important definitions

- Simple weaning: refers to patients who can be successfully extubated after the first weaning test
- Difficult weaning: patients who require up to three Spontaneous breathing trial SBTs (or as long as 7 days) to be successfully extubated.
- Prolonged weaning: applies to patients who exceed the limits of difficult weaning.

Risk factors of extubation failure

- Impaired neurological status
- Poor cough
- Increased secretion
- High APACHE score at the time of weaning
- Positive fluid balance
- High Risk for failure population
    - Age > 65 ys
    - Chronic respiratory disease
    - Chronic cardiac disease

Assessment of readiness to wean

- Clinical assessment
    - Resolution of acute phase of disease for which patient was intubated.
    - Adequate cough
    - Absence of excessive tracheobronchial secretion
- Objective criteria
    - Adequate oxygenation: $PaO_2>60$ mmHg with PEEP ≤ 8 cmH_2O, $SaO_2≥90\%$, $FIO_2≤0.5$, $PaO_2/FIO_2 > 200$
    - Respiratory rate < 30 /min

- PH and PaCO2 appropriate for patients' baseline respiratory status.
- Hemodynamically stable: minimal or no vasopressor /inotropes, no evidence of myocardial ischemia
- HR< 140 beats/min
- Patient is arousable or Glasgow Coma Scale (GCS) ≥ 13

Spontaneous breathing trial

- The SBT can be conducted through
  - Ventilator
    - Use pressure support (PS) ventilation of 5-7 cmH2O + low PEEP level (5 cmH2O)
    - The advantage is patient safety as patient is not disconnected from ventilator with monitoring of tidal volume and respiratory rate
  - T-Piece
    - Deliver oxygen enriched gas at high flow rate through a horizontal arm of the T-shaped circuit
- Protocol for SBT
  - Allow 30 to 120 minutes of initial trial of spontaneous breathing
  - Increase the FIO2 by 10% for the period of spontaneous breathing
  - For case of short-term ventilator support (post surgery), a successful one-hour of spontaneous breathing is enough to discontinue ventilation
  - SBT is considered failure when patients develop respiratory, cardiovascular, or neurological disability.
- Criteria of successful SBT
  - Gas exchange acceptable (SPO2≥90%; PaO2≥60 mmHg; PH ≥ 7.32; increase in PaCO2 ≤ 10 mmHg from the start of the trial
  - Stable respiratory rate (RR ≤ 30-35 breaths /min, change in RR < 50%)
  - Hemodynamically stable (HR < 120-140, HR increase by less than 20%, SBP > 90 mmHg and < 180 mmHg, change in SBP < 20%
  - No significant change in mental status, anxiety, or agitation
  - No diaphoresis or sign of increased work of breathing (use of accessory muscle, dyspnea, paradoxical breathing)
- Failure of SBT
  - Increase ventilator setting to previously tolerated level or higher if necessary until patient stable again and wait 24 hours before trying again
  - Search for potential reversible etiology
  - Use pressure support ventilation as weaning tool by gradually reducing pressure support by 2 cmH2O once or twice a day as tolerated

- Once pressure support is reduced to 10 cmH2O, repeat SBT daily until the patient can be successfully extubated

Extubation

Before extubation assess patient's ability to protect and maintain airway

- Level of consciousness
- Cough strength
- Quantity of secretion and frequency of suction. Probability of failed extubation increases with increase secretion and frequent suction interval
- Airway patency- cuff leak test. (Patients with prolonged intubation, or difficult/traumatic intubation are at risk of post-extubation upper airway obstruction.
    - Cuff leak test:
        - Change to volume-cycled ventilation then deflate cuff and measure the difference between inspired and expired tidal volumes.
        - Average the lowest three tidal volumes over 6 breaths and substract that from inspired tidal volume→ give you the cuff leak volume
        - Cuff leak volume < 110 ml or <12-24% of delivered tidal volume is the threshold of determination of decrease airway patency

Weaning failure

- In difficult weaning, do thorough diagnostic test to exclude respiratory pump failure versus cardiac pump failure versus muscle weakness.
- In prolonged weaning, Consider tracheostomy for increased patient comfort
- In High Risk for failure population, a specialized algorithm is suggested to minimize the risk of extubation failure (figure 17).

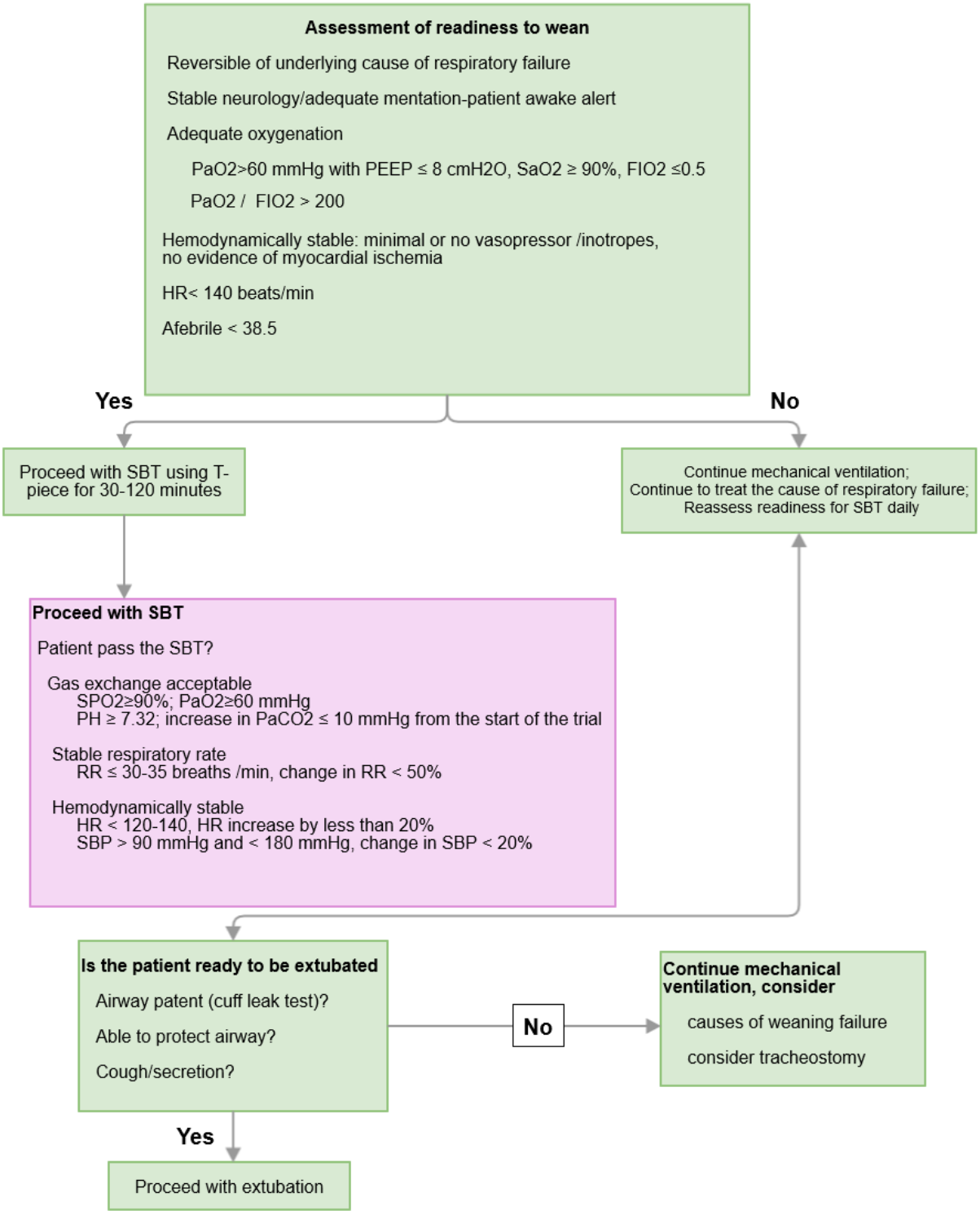

Figure 20: Weaning Algorithm

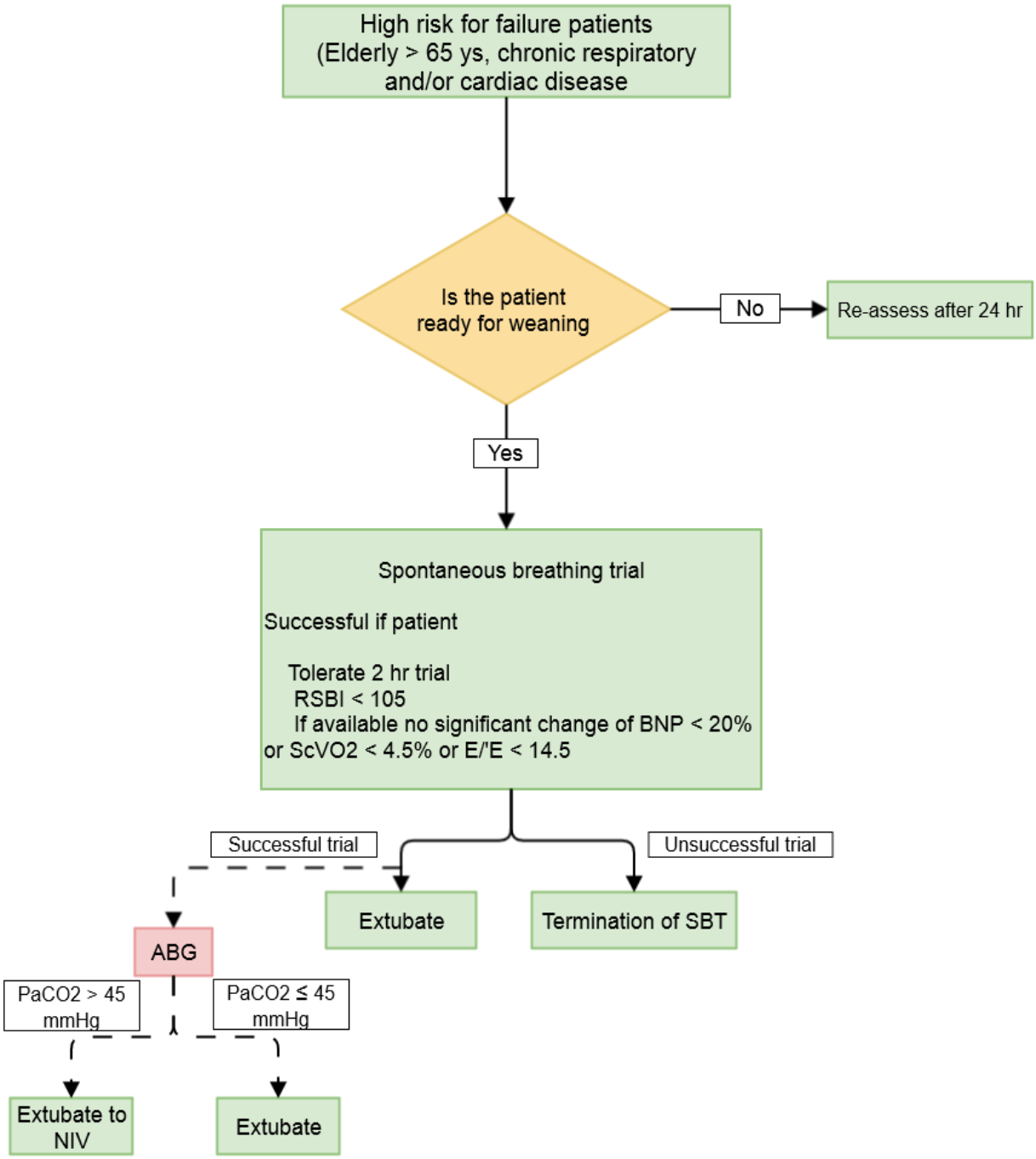

Figure 21: Weaning strategy for high risk for failure population [3]

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Non-invasive ventilation protocol

Indications of NIV

- Bedside observation
  - Increase dyspnoea moderate to severe
  - Tachypnoea (>24 bpm in obstructive, >30/ min in restrictive)
  - Signs of increased work of breathing, accessory muscle use, and abdominal paradox
- Gas exchange
  - Acute or acute on chronic ventilatory failure (best indication), $PaCO_2 > 50$ mmHg, PH < 7.35
  - Hypoxaemia (use with caution), $PaO_2/FIO_2 < 200$

Specific indication of NIV

- Chronic obstructive pulmonary disease
  - it is now considered the first-line therapy in COPD and there is growing evidence that its use may be applicable in patients with severe acidaemia (pH<7.25) and hypercarbic coma
- Cardiogenic pulmonary oedema
  - There is good evidence to support the use of both CPAP and NPPV in acute pulmonary oedema
- Pneumonia
  - **NOT recommended** to be used in patient with pneumonia except in COPD patient
- Lung contusion/chest trauma
  - Respond well to NIV and may improve mortality
- Neuromuscular disorder
  - **NOT recommended** in acute neuromuscular disorders such as Guillain–Barré syndrome and acute myasthenia because of high incidence of aspiration.
  - May be used in Chronic neuromuscular disorders, notably motor neurone disease (MND) as it improves quality of life
- Post extubation in intensive care
  - **NOT recommended** to treat post extubation respiratory failure
  - It could be used as a tool to help wean patients deemed not suitable for extubation from MV
  - The use of CPAP both prophylactically and as a treatment for hypoxic respiratory has been demonstrated to reduce reintubation rates and mortality in after open abdominal visceral surgery

Contraindication of NIV

- Agitation
- Glasgow<12 (the exception being suitable "do not intubate" unconscious patients with hypercapnic COPD)
- Ineffective cough
- Airway obstruction
- Distended abdomen
- Vomiting
- Upper GI bleeding
- Hemodynamic instability
- Complex arrhythmia
- Facial trauma
- Esophageal surgery
- Undrained barotrauma

Initiation and titration of therapy

- Initial settings for Bilevel Positive Airway Pressure (BPAP) : Inspiratory Positive Airway Pressure (IPAP) of 10cmH2O and Expiratory Positive Airway Pressure (EPAP) of 4-5cmH2O= Pressure Support (PS) level of 5-6cm H2O
- Initial settings for Continuous Positive Airway Pressure (CPAP)
- Increases to IPAP of 2-5cmH2O can be undertaken every 10 minutes or as clinically indicated, until therapeutic response is achieved. The maximum IPAP should not exceed 20 – 23 cmH2O.
- Optimal Non-invasive Positive Pressure Ventilation (NIV) is the lowest pressure and lowest Fi02 that achieve Sa02 of 90% or Pa02 of 60mmHg without further clinical deterioration
- If the patient does not clinically improve within four hours of starting NIV, the decision to intubate and ventilate is to be made

Oral feeding and nutrition during NIV

- Oral feeding is to be initiated if the patient is able to tolerate small periods off NIV.
- No oral intake is to be implemented if the patient has a decreased LOC or in respiratory distress with an increased work of breathing (i.e. R.R > 30/min). Intravenous fluids are to be commenced.
- Patients receiving NIV are to have a strict fluid balance and stool chart implemented for the duration of their NIV therapy, to assess for elimination and fluid status

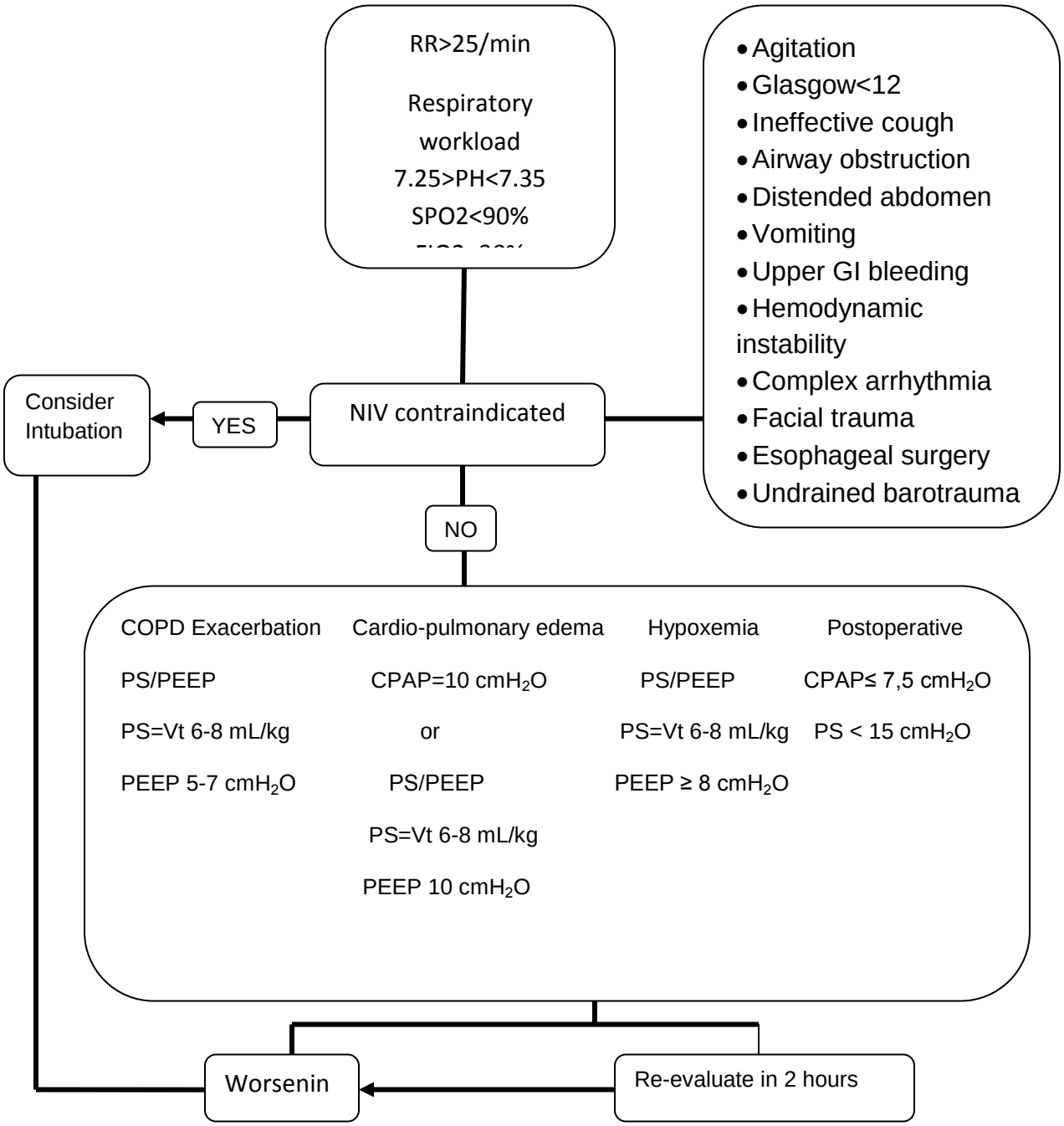

Figure 22: Non-Invasive ventilation Algorithm

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Nutrition Protocol

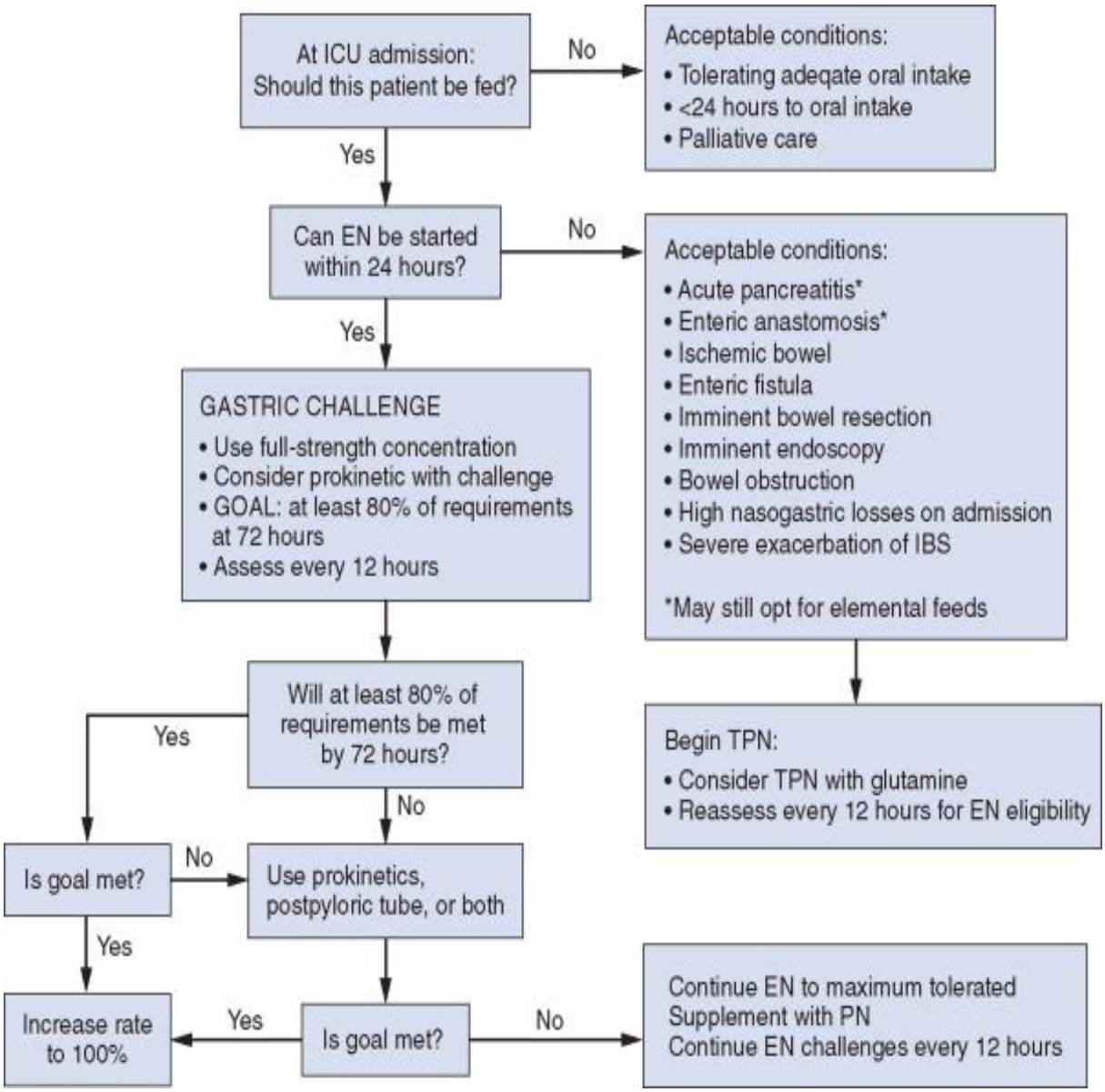

Figure 23: Stepwise Enteral Nutritional Algorithm

Estimation of Nutritional Requirement

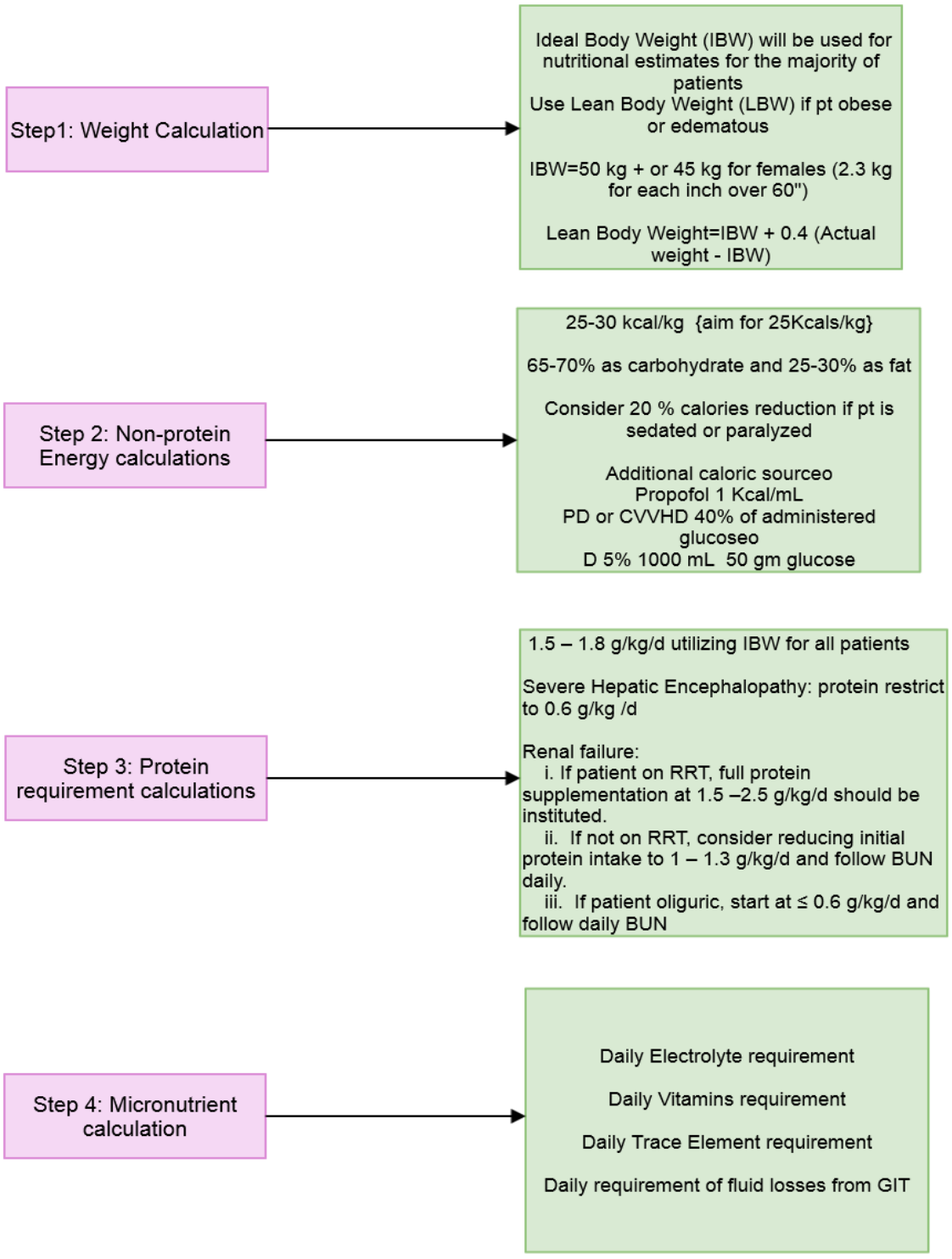

Figure 24: Estimation of nutritional requirement

Table 4: Daily requirement of micronutrients

Table: Daily requirement of micronutrients		
Sodium	1.0 mmol/kg/day	
Potassium	1.0 mmol/kg/day	Dependent on renal function
Phosphate	0.2 mmol/kg/day	Dependent on renal function
Magnesium	0.3 mmol/kg/day	Dependent on renal function
Calcium	0.1 mmol/kg/day	
Vitamins	B groups daily B12, Folate, A, D, E, K weekly	Trace elements as required.
Replacement solutions	1. Urine 2. Nasogastric/ileostomy 3. Pancreatic/biliary fistulae	1.½ Normal saline ± KCl 10 ml/L 2. ½ Normal saline ± KCl 10 ml/L 3. Ringer Lactate or Acetate

Enteral Feeding

1. Start enteral feeding within 24-48 hours of ICU admission if the GIT is functioning and the patients have been adequately resuscitated.
2. For patients who have undergone recent bowel anastomosis, discussion between surgeon and intensivist may be required before starting enteral feeding
3. Enteral feedin will be carried out using nasogastric or orogastric tube. Use 12-14 F in adult and confirm the correct position by any two of the following methods
    a. Gastric content aspiration
    b. Auscultation of epigastric area after injecting 10-20 mL of air down the tube
    c. X-ray
4. Use any of the following methods to administer enteral feeding
    a. Continuous feeding

    b. Intermittent bolus feeding

5. Withhold enteral feeding in the following conditions
    a. Any procedure involving the airway or gastrointestinal tract
    b. Planned extubation specially for high risk if reintubation or anticipated difficult airways
    c. In the setting of hemodynamic compromise (**patients requiring significant hemodynamic support, including high-dose catecholamine agents, alone or in combination with large volume fluid or blood product resuscitation to maintain cellular perfusion**), EN should be withheld until the patient is fully resuscitated and/or stable
6. Enteral formula preparation and hanging time
    a. Sterile water should be used for formula reconstitution, medication dilution, and tube flush
    b. Duration for hanging time
        i. For ready to hang formula the duration of hang time ranging from 24-48 hr according to manufacturer recommendation
        ii. For sterile decanted formula the duration of hang time is 8 hr
        iii. For powdered reconstituted formula the duration of hang time is 4 hr
    c. For open system change the administration sets every 24 hr
    d. Opened unused formula must be refrigerated and discarded within 24 hr
7. Calories and protein requirement
    a. Non-protein calorie should be provided at 20-25 kcal/kg/day
    b. Protein should be supplied at least 1-1.5 g/kg/day
8. Enteral feeding intolerance
    a. Monitor patient's GIT tolerance to feeding every 4 hours look for

i. Diarrhea
ii. Abdominal distension
iii. High gastric residue aspirate
iv. Multiple emetic episodes

b. Consider nasojejunal feeding in patients with feeding intolerance or pancreatitis
c. IV metochlopramide 10-20 mg/8 he and Erythromycin 250 mg/12 enhance motility

Parenteral Nutrition

Indication

1. PN should not be initiated in the immediate postoperative period, but should be delayed for 5-7 days
2. If there is evidence of protein calorie malnutrition (recent weight loss > 10-15% or actual body weight < 90% of IBW) on admission and EN is not feasible, initiate PN as soon as possible
3. If a patient is malnourished and is expected to undergo major upper GI surgery and EN is not feasible, initiate PN 5-7 days preoperatively and continue it into the postoperative period
4. In high output enterocutaneous fistulae, initiate PN early if more than 60% of energy needs are not met with EN after 2 days

Administration

a. High osmolarity PN through central line
b. Low osmolarity (<850 mOsmol/L) PN can be administrated through dedicated peripheral venous line

Components

a. Non-protein calorie should be provided at 20-25 kcal/kg/day
b. Protein should be supplied at least 1-1.5 g/kg/day
c. Lipids are provided at 0.7-1.5 g/kg/day
d. Glucose : fat calorie ratio are around 60:40 or 70:30 of non-protein calories in order to avoid hyperlipidemia
e. Daily dose of multivitamins and trace element should be included
f. Electrolyte is added according to serum levels

Monitoring

a. Blood glucose level every 4 hours
b. Daily renal profile

c. Biweekly liver function tests, phosphate, magnesium, and serum calcium level
d. Catheter related blood stream infection

Nutrition therapy in special population

Obese patients

a. For all classes of obesity where BMI is >30, the goal of the energy goal should not exceed 60% to 70% of target energy requirements or 11–14 kcal/kg actual body weight/day (or 22–25 kcal/kg ideal body weight/day)
b. Proteins are provided at ≥ 2 g/kg IBW/day for BMI 30-40 and at ≥ 2.5 g/kg IBW/day for BMI ≥ 40

Burns

a. Glucose is provided at 5-7 mg/kg/min which represents 50% of total caloric intake
b. Protein are provided at 1.5-2 g/day

Liver failure

a. Provide energy requirement at 1.3 normal requirement
b. Protein should be provided at1.5 – 1.8 g/kg/d utilizing IBW for all patients
b. Severe Hepatic Encephalopathy: protein restrict to 0.6 g/kg /d

Respiratory failure

a. Specially high-lipid low-carbohydrate formulations designed to manipulate the respiratory quotient and reduce CO2 production **ARE NOT RECOMMENDED** for routine use in ICU patients with acute respiratory failure.
b. Provide formulation characterized by an antiinflammatory lipid profile (i.e., omega-3 fish oils, borage oil) and antioxidants

Acute Kidney injury

a. Patients receiving hemodialysis or continuous renal replacement therapy should receive increased protein, up to a maximum of 2.5 g/kg/day
b. Protein should not be restricted in patients with renal insufficiency as a means to avoid or delay initiation of dialysis therapy.

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Prophylaxis of Deep Venous Thrombosis

General Principles

- Pharmacologic methods are the most effective methods against DVT prophylaxis
- Mechanical methods of prophylaxis should be used routinely in whom pharmacological prophylaxis is contraindicated
- Elastic stockings are considered the least effective methods of DVT prophylaxis and should never be used alone in moderate to high risk of DVT
- Intermittent pneumatic compression is more effective than elastic stockings and can be used alone as a replacement for pharmacological prophylaxis in patients who are bleedings or who have high risk of bleeding.

Clinical risk factors for thromboembolism in critically ill patients

- Recent surgery
- Trauma
- Burn
- Malignancy
- Sepsis
- Stroke, spinal cord injury
- Age > 40 years
- Obesity
- Mechanical ventilation

Risk factors of bleeding

- Active bleeding
- Acquired bleeding disorder (acute liver failure)
- Use of anticoagulants
- Acute stroke
- Thrombocytopenia (platelets < 50.000)
- Uncontrolled systolic hypertension (> 230/120 mmHg)
- Inherited bleeding disorder (e.g. Hemophilia)

Protocol of thromboembolism prophylaxis

- Assess all patients on ICU admission for risk of thrombosis and risk of bleeding and subsequently daily.
- Provide thromboembolism prophylaxis to all patients admitted to ICU according to reason of admission, taking in account
    - Any planned interventions

- The use of other therapies that may increase risk of bleeding

- For neurosurgical patients, mechanical methods of prophylaxis are favoured. However the use of heparin products is considered safe after 48 to 72 hrs.
- It is recommended to withhold pharmacological prophylaxis for 2 weeks after thrombotic stroke and 1 week after embolic stroke.
- Withhold pharmacological prophylaxis with significant decrease in platelet count (30-50% initial count), thrombocytopenia (<50000/mm^3) or INR > 1.5
- The insertion and removal of epidural catheter should follow guidelines (see table)

Pharmacological prophylaxis

- Low dose unfractionated heparin (LDUH)
  - Recommended dose: 5000 units SC /8-12 hr.
  - Stop LDUH 4 to 6 hr prior to elective surgery.
  - Table .... use of LDUH in neuroaxial blockade.
- Low molecular weight heparin (LMWH) (Enoxaparin)
  - Recommended dose
    - Prophylaxis: CrCl ≥ 30ml/min → 40 mg SC /24 hrs
      CrCl < 30ml/min → 30 mg SC /24 hrs
    - Therapeutics: CrCl ≥ 30ml/min → 1 mg/kg SC Q12H
      CrCl < 30ml/min → 1 mg/kg SC once daily
  - Stop LMWH 24 hrs before elective surgery
  - In obese patients with BMI > 40
    - Prophylaxis: 1 mg/kg ideal + 25% (actual body weight- ideal body weight)
    - Therapeutic: 1 mg/kg/12 based on actual body weight
  - Table... describe the use of LMWH in neuroaxial blockade
- Fondaparinux
  - Recommended dose
    - Prophylaxis: 2.5 mg SC /24 hrs
    - Therapeutics: 7.5 mg SC/ 24
  - Contraindicated Cr Cl < 30 ml/min
  - Stop fondaparinux 2 to 4 days prior to elective surgery in patients with normal renal function

Table 5: perioperative anticoagulation for epidural anesthesia

	LDUH	Enoxaparine		Fondaparinux
Insertion of catheter	4 hrs after last dose	Single-daily dose 12 hrs after last dose	Twice-daily dose No recommendation Delay block for 24 hrs	No recommendation
Removal of catheter	4 hrs after last dose	12 hrs after last dose	NA	36 hrs after last dose
Subsequent dose after removal	1 hr	4 hrs	4 hrs	12 hrs
Traumatic puncture	Initiate prophylaxis after 6 hr	Consider initiating prophylaxis after 24 hrs	NA	Single shot spinal is safe but avoid epidural analgesia

Contraindications to the use of graded compression

- Arterial insufficiency
- Absent peripheral pulse
- Deep vein thrombosis
- Lower extremity ischemia/gangrene

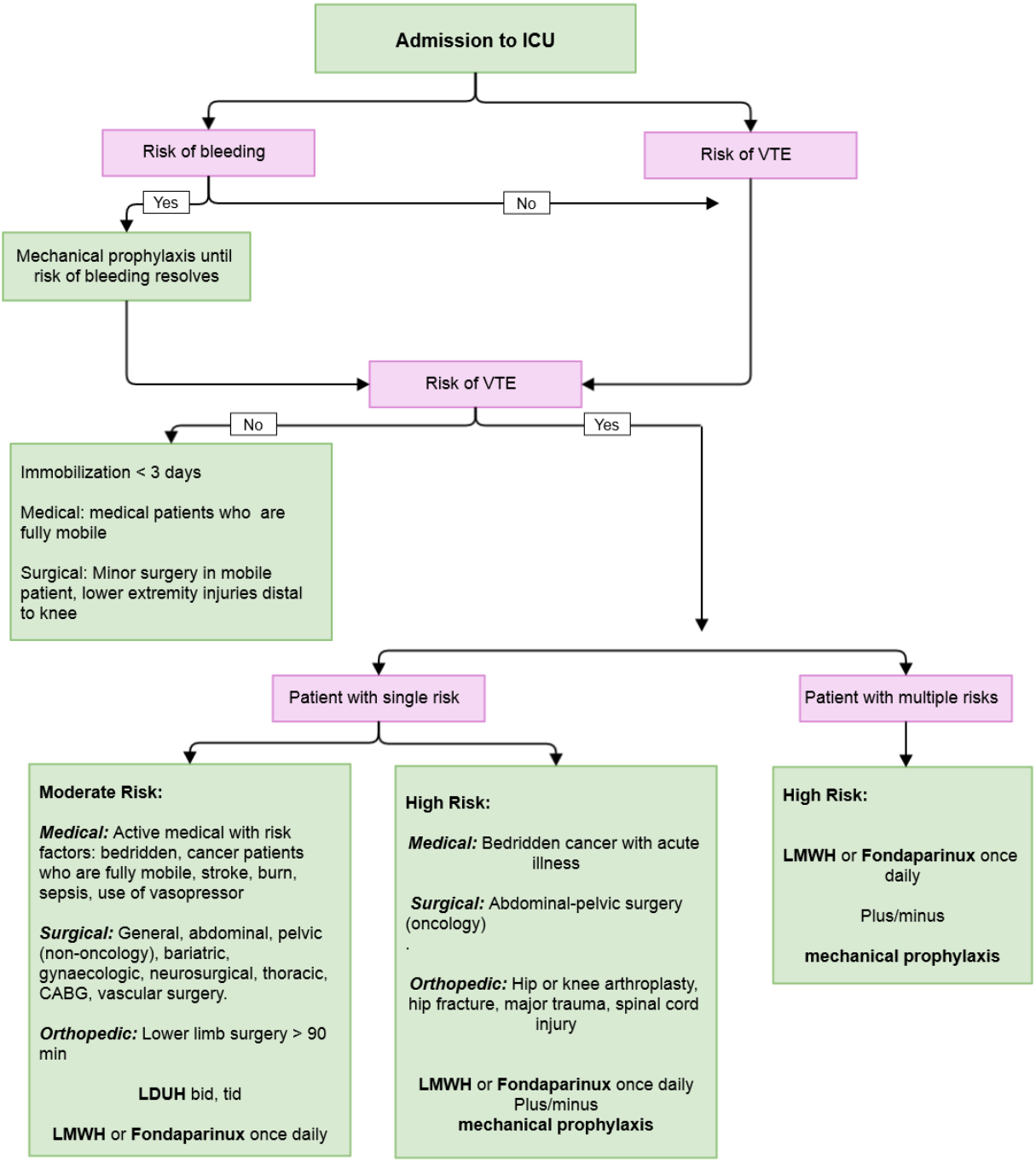

Figure 25:VTE prophylaxis protocol

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Management of Acute Pulmonary Embolism

Clinical classification of pulmonary embolism

The stratification of severity of pulmonary embolism (PE) is based on the patient's clinical status at presentation

1. High risk pulmonary embolism: Defined as systolic blood pressure < 90 mmHg, or a systolic pressure drop by > 40 mmHg, for > 15 minutes
2. Not-high risk pulmonary embolism

Diagnostic strategies

The diagnostic algorithms for suspected PE—with and without shock or hypotension is demonstrated in figures 1 and 2

Treatment in acute phase

Pulmonary embolism with shock or hypotension (high-risk pulmonary embolism)

I. Hemodynamic and respiratory support
   1. Correct systemic hypotension using norepinephrine or epinephrine
   2. Fluid challenge 500 mL (avoid aggressive fluid resuscitation).
   3. Start O2 therapy to correct hypoxemia , if mechanical ventilation is required keep end – inspiratory plateau pressure <30 cmH_2O & PEEP should be applied cautiously

II. Antocoagulation
   1. Intravenous unfractionated heparin (UFH) should be administered.
   2. LMWH or fondaparinux have not been tested in the setting of hypotension and shock

III. Primary reperfusion therapy
   1. Systemic thrombolysis.
   2. Surgical embolectomy is recommended when thrombolysis is contraindicated.

Pulmonary embolism without shock or hypotension (intermediate- or low-risk pulmonary embolism)

I. Anticoagulation
   1. Low molecular weight heparin (LMWH) or fondaparinux, given subcutaneously at weight-adjusted doses without monitoring, is the treatment of choice unless there is severe renal dysfunction

II. Risk stratification
   1. In patients without shock, risk assessment should begin with a validated clinical score, preferably the simplified pulmonary embolism severity index sPESI.
      a. Patients with sPESI=0 are considered low-risk patients and early discharge with outpatient treatment should be considered

b. Patients with sPESI ≥ 1 are considerd intermediate risk. These patients are further classified into
    i. Intermediate-high risk group:
        - Patients with acute PE, an echocardiogram or CT scan indicating RV dysfunction, and a positive cardiac troponin test.
        - Systemic thrombolysis is not routinely recommended as primary treatment for patients with intermediate-high-risk PE, but should be considered if clinical signs of hemodynamic decompensation appear.
    ii. Intermediate-low risk group: Patients in whom the echocardiogram (or CT angiogram) or the cardiac troponin test—or both—are normal. Anticoagulation is indicated
        - Anticoaulation is indicated
        - Primary reperfusion treatment IS NOT indicated.

IV. Thrombolytic therapy
1. Indicated in high risk pulmonary embolism (shock or hypotension)
2. The approved regimens for thrombolytic therapy are shown in table 1
3. Contraindications to thrombolytic therapy are
    a. Absolute contraindication
        - Any prior intracranial hemorrhage
        - known structural intracranial cerebrovascular disease (eg, arteriovenous malformation)
        - Known malignant intracranial neoplasm
        - Ischemic stroke within 3 months
        - Suspected aortic dissection
        - Bleeding or bleeding diathesis
        - Recent surgery encroaching on the spinal canal or brain, and recent significant closed-head or facial trauma with radiographic evidence of bony fracture or brain injury
    b. Relative contraindications
        - age > 75 years
        - Current use of anticoagulation
        - Pregnancy;
        - Noncompressible vascular punctures;
        - Prolonged cardiopulmonary resuscitation (10 minutes)

- Recent internal bleeding (within 2 to 4 weeks)
- History of chronic, severe, and poorly controlled hypertension; severe uncontrolled hypertension on presentation (systolic blood pressure > 180 mm Hg or diastolic > blood pressure 110 mm Hg)
- Remote (>3 months) ischemic stroke
- Major surgery within 3 weeks.

4. Unfractionated heparin infusion should be stopped during administration of streptokinase or urokinase; it can be continued during rtPA infusion
5. In patients receiving LMWH or fondaparinux at the time that thrombolysis is initiated, infusion of UFH should be delayed until 12 hours after the last LMWH injection

Table 6: approved regimens for thrombolytic therapy in acute PE

Agent	Dosage	Precautions
Streptokinase	250000 IU over 30 min Then 100000 IU/hour X 24 hours	• Unfractionated heparin (UFH) should not be given concomitantly with fibrinolytic therapy in acute massive PE. • After fibrinolytic therapy, anticoagulation treatment is recommended to prevent recurrent thrombosis. • Do not begin heparin until the activated partial thromboplastin time (aPTT) has decreased to less than twice the normal control value
Urokinase	4400 U/kg/10 min 4400 U/kg X 12-24 hours	
Altepase (tPA)	Patient weight < 67 kg • 15 mg I.V. bolus followed by 0.75 mg/kg over the next 30 minutes (Max 50 mg) and then 0.5 mg/kg over the next 60 minutes (Max 35 mg). Patients weight >67 kg • 15 mg I.V. bolus followed by 50 mg over the next 30 minutes and then 35 mg over the next 60 minutes	

V. Anticoagulation

1. The standard duration of anticoagulation should cover at least 3 months.
2. Acute-phase treatment consists of administering parenteral anticoagulation [unfractionated heparin (UFH), LMWH or fondaparinux] over the first 5–10 days.
3. Parenteral heparin should overlap with the initiation of a vitamin K antagonist (VKA); alternatively, it can be followed by administration of one of the new oral anticoagulants
4. LMWH and fondaparinux are preferred over UFH for initial anticoagulation in PE
5. UFH is recommended for patients in whom primary reperfusion is considered, aswell as for those with serious renal impairment (creatinine clearance ,30 mL/min), or severe obesity.
6. The LMWHs approved for the treatment of acute PE are listed in Table.....
7. Oral anticoagulants should be initiated as soon as possible, and pref- erably on the same day as the parenteral anticoagulant.

8. Anticoagulation with UFH, LMWH, or fondaparinux should be continued for at least 5 days and until the international normalized ratio (INR) has been 2.0–3.0 for two consecutive days
9. Warfarin can be started at a dose of 10 mg in younger (e.g. ,60 years of age), otherwise healthy outpatients, and at a dose of 5 mg in older patients and in those who are hospitalized.
10. Patients with PE should receive at least 3 months of anticoagulant treatment

Table 7: Low-molecular-weight heparins and pentasaccharide (fondaparinux) approved for the treatment of pulmonary embolism

	Dosage	Interval
Enoxaparin	1.0 mg/kg or 1.5 mg/kg[a]	Every 12 hours Once daily[a]
Dalteparin	100 IU/kg Or 200 IU/kg	Every 12 hours Once daily
Fondaparinux	5 mg (body weight <50 kg); 7.5 mg (body weight 50–100 kg); 10 mg (body weight >100 kg)	Once daily

[a] Once-daily injection of enoxaparin at the dosage of 1.5 mg/kg is approved for inpatient (hospital) treatment of PE in the United States and in some, but not all, European countries

VI. Inferior vena cava filter
1. Adult patients with any confirmed acute PE (or proximal DVT) with contraindications to anticoagulation or with active bleeding complication should receive an IVC filter
2. For patients with recurrent acute PE despite therapeutic anticoagulation
3. IVC filter may be considered for patients with acute PE and very poor cardiopulmonary reserve, including those with massive PE
4. An IVC filter should not be used routinely as an adjuvant to anticoagulation and systemic fibrinolysis in the treatment of acute PE
5. Anticoagulation should be resumed in patients with an IVC filter once contraindications to anticoagulation or active bleeding complications have resolved

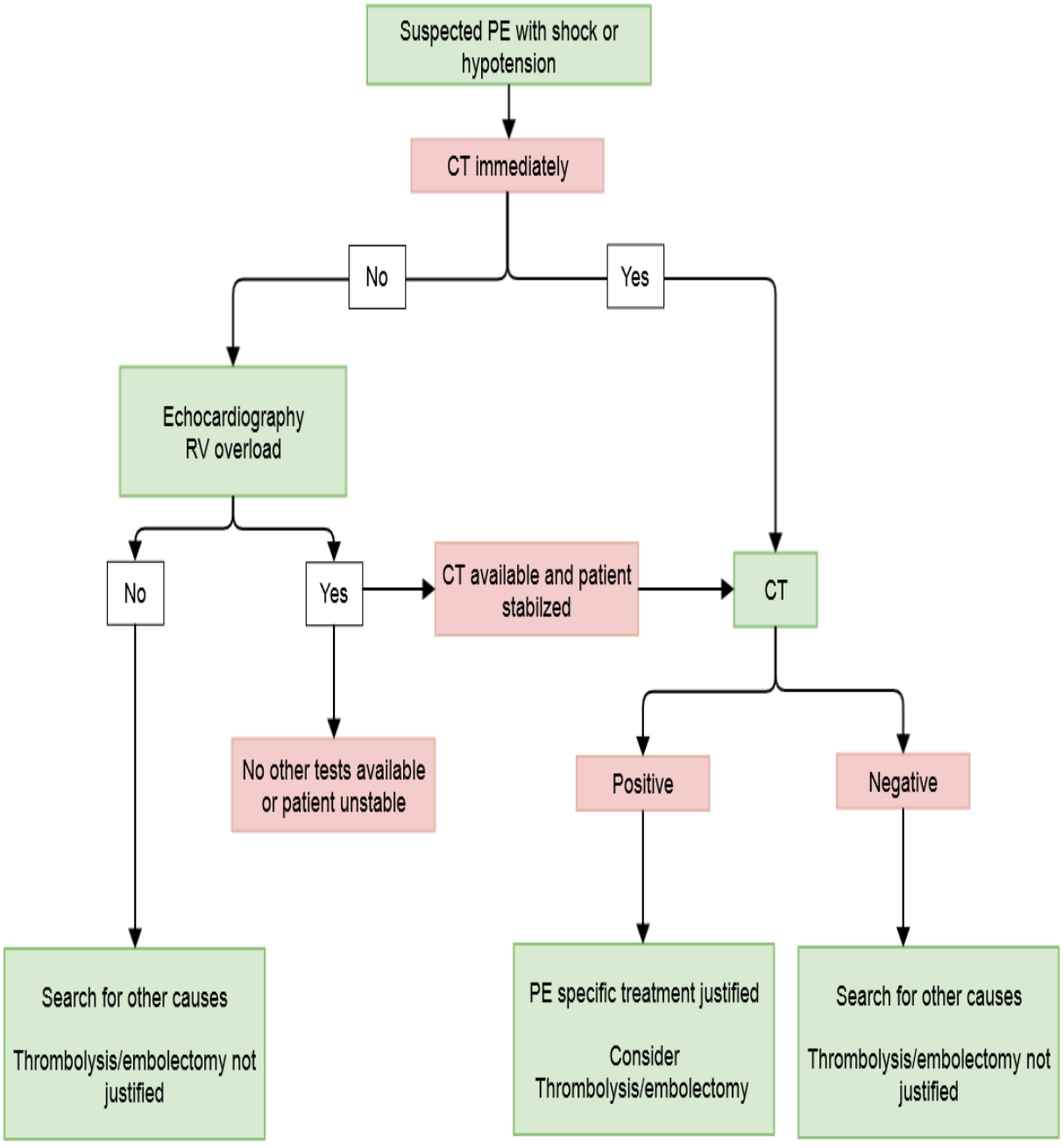

Figure 26: Proposed diagnostic algorithm for patients with suspected high-risk PE

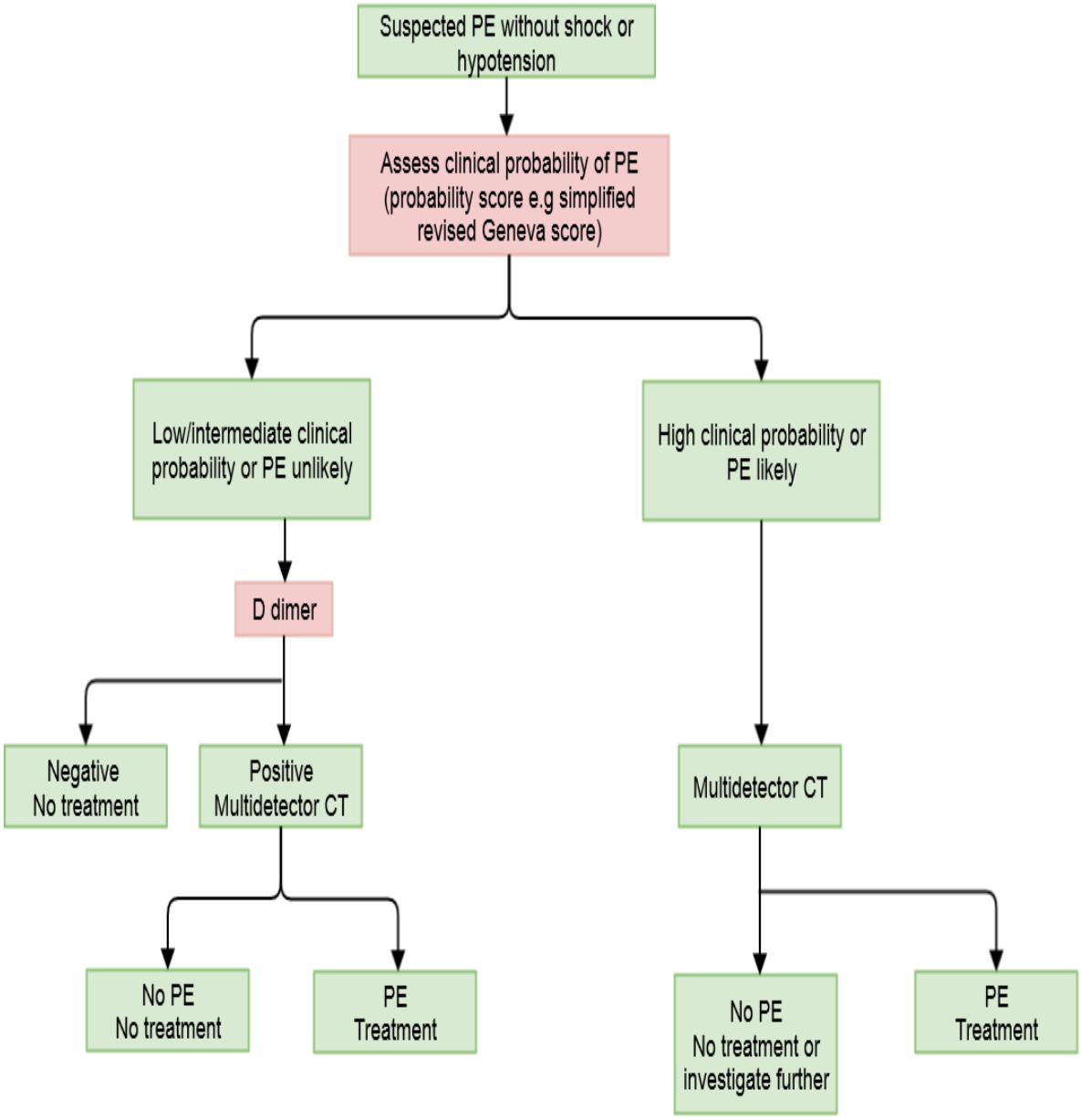

Figure 27: Proposed diagnostic algorithm for patients with suspected non-high-risk PE

Table 8: simplified revised Geneva score for prediction of PE

Items	Clinical decision rule points
Simplified Revised Geneva score	
Previous PE or DVT	I
Heart rate 75–94 b.p.m. ≥95 b.p.m	 I 2
Surgery or fracture within the past month	I
Haemoptysis	I
Active cancer	I
Unilateral lower limb pain	I
Pain on lower limb deep venous palpation and unilateral oedema	I
Clinical probability	
Three-level score	
Low	0–1
Intermediate	2–4
High	≥5
Two-level score	
PE unlikely	0–2
PE likely	≥3

Table 9: Simplified pulmonary injury severity index

Items	Clinical decision rule points
Simplified pulmonary embolism severity index	
Age in years	I point (if age > 80 years)
Cancer	I point
Chronic heart failure	I point
Chronic pulmonary disease	
Hear rate > 110 bpm	I point
Systolic blood pressure < 100 mmHg	I point
Arterial oxygen saturation < 90%	I point
Risk Strata	
0 point	30 day mortality 1%
≥ 1 point	30 day mortality 10%

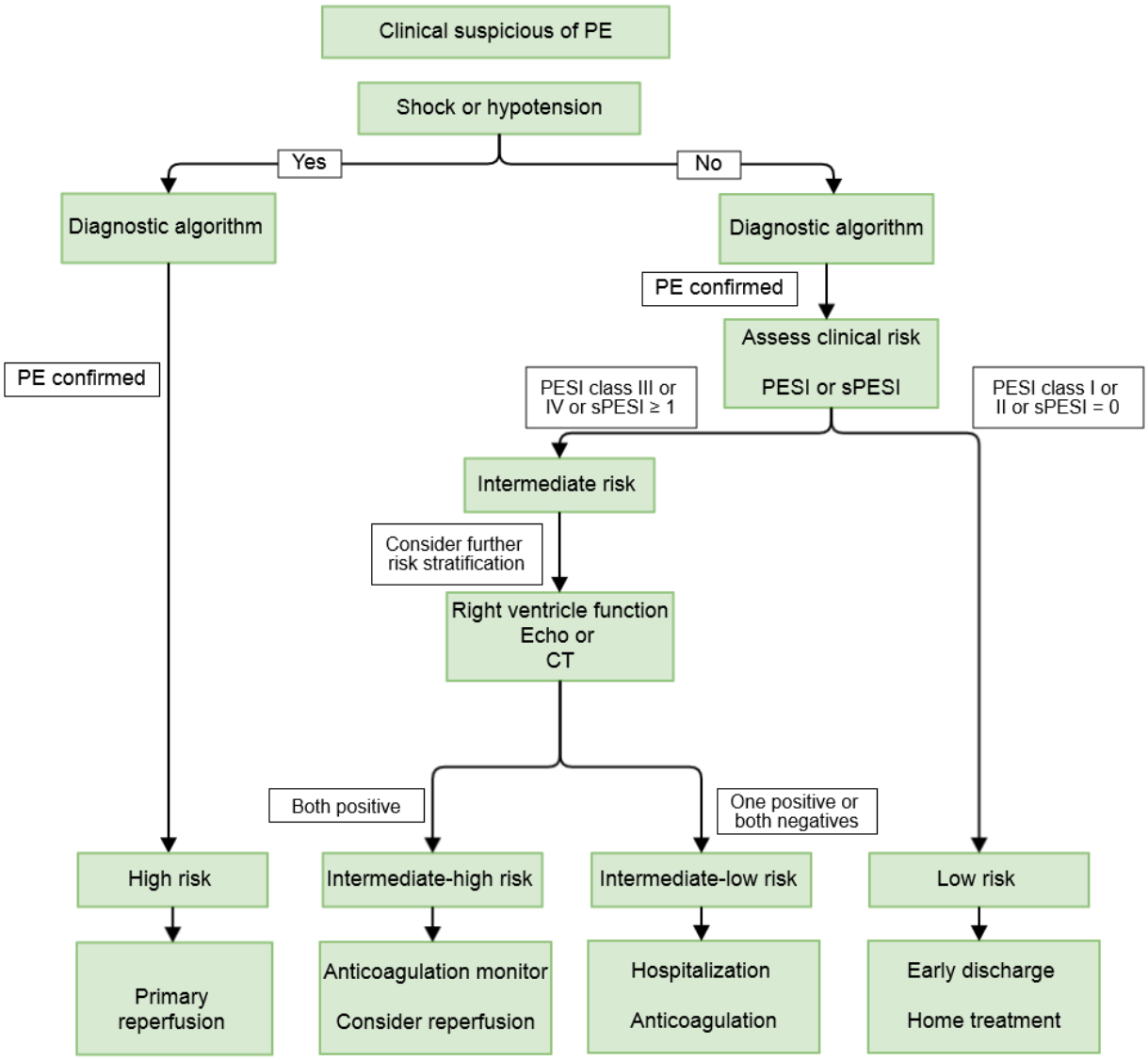

Figure 28: Risk-adjusted management strategies in acute PE

References

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Fluid Therapy And Electrolyte Replacement Protocol

a) **Maintenance fluids**

I. Usually crystalloids:
- 5% dextrose + 1/2 N. Saline
- 5% dextrose / N. Saline
- 1/2 N. Saline
- Ringer Lactate
- Ringer Acetate

II. Usual volumes: 25-30 ml/kg/day → 80-120 ml/hr

III. TPN (refer to guidelines)

b) **Replacement / resuscitation fluids**

I. N.saline should be used for most fluid resuscitation.
- Equivalent to 5% albumin for resuscitation
- Better for patients with head trauma.

II. Colloid (5% albumin, gelatins, and Hydroxyethyl starch 6% 130/0.4) may be considered for fluid resuscitation in selected patients.

III. Blood and blood component therapy as indicated and according to Transfusion guidelines. (See transfusion therapy protocol)

IV. Crystalloid replacement is usually used for excessive renal, enteric and burns losses.

Table: Fluids for intravenous replacement of extracellular volume or water deficit.				
	[Na+] (meq/L)	[Cl^-] (meq/L)	[osm] (mosm/L)	Other
0.9% NaCl (normal saline)	154	154	308	
5% dextrose in 0.9% NaCl	154	154	560	Glucose, 50 g/L
Ringer's lactate	130	109	273	K+, Ca2+, lactate1
5% dextrose in water	0	0	252	Glucose, 50 g/L
0.45% NaCl	77	77	154	
5% dextrose in 0.45% NaCl	77	77	406	Glucose, 50 g/L
6% hetastarch in 0.9% NaCl	154	154	308	
5% albumin	160-130	160-130	330	

Table: Guidelines for replacement of fluid losses from the gastrointestinal tract.		
	Replace mL Per mL with	Add
Gastric (vomiting or nasogastric aspiration)	0.45% NaCl	KCl, 10 meq/L
Small bowel	0.45% NaCl	KCl, 10 meq/L
Biliary	Ringer Lactate or acetate	
Large bowel (diarrhea)	0.45 NaCl	KCl, 20 meq/L
Urine	0.45% NaCl	KCl, 10 meq/L

Electrolyte Replacement Protocol

Patients must meet the following criteria prior to initiation of the Potassium, Magnesium, or Phosphorus protocols:

- SCr < 2 mg/dL
- Weight > 40 kg

POTASSIUM REPLACEMENT PROTOCOL – INTRAVENOUS

- Recommended rate of infusion is 10 mEq/h
- Maximum rate of intravenous replacement is 20 mEq/h with *continuous ECG monitoring* (the maximum rate may be increased to 40 mEq/h in emergency situations
- Maximum Concentration for Central IV administration = 20 mEq/50 mL
- Maximum Concentration for Peripheral IV administration = 10 mEq/50 mL

Current Serum Potassium Level	Central IV administration	*Peripheral* IV Administration	Monitoring
3.6 – 3.9 mEq/L	20 mEq IV over 2 HR x 1	10 mEq IV over 1 HR x 2	No additional action
3.4 – 3.5 mEq/L	20 mEq IV over 2 HR x 1 **AND** 10 mEq IV over 1 HR x 1	10 mEq IV over 1 HR x 3	No additional action
3.1 – 3.3 mEq/L	20 mEq IV over 2 HR x 2	10 mEq IV over 1 HR x 4	Recheck serum potassium level 2 hours after infusion complete
2.6 – 3 mEq/L	20 mEq IV over 2 HR x 2 **AND** 10 mEq IV over 1 HR x 1	10 mEq IV over 1 HR x 5	Recheck serum potassium level 2 hours after infusion complete
2.3 – 2.5 mEq/L	20 mEq IV over 2 HR x 3	10 mEq IV over 1 HR x 6	Recheck serum potassium level 2 hours after infusion complete
< 2.3 mEq/L	**Call Physician AND** 20 mEq IV over 2 HR x 3	**Call Physician AND** 10 mEq IV over 1 HR x 6	Recheck serum potassium level 2 hours after infusion complete
• If both potassium and phosphorus replacement required, subtract the mEq of potassium given as potassium phosphate from total amount of potassium required. (Conversion: 3 mmols KPO = 4.4 mEq K^+)			

POTASSIUM REPLACEMENT PROTOCOL – ORAL or ENTERAL (PT)

- Standard dosage forms: KCl 20mEQ tablet or KCl 10% solution (20 mEq/15 mL)

Current Serum Potassium Level	Total Potassium Replacement	Monitoring
3.7 – 3.9 mEq/L	20 mEq KCl PO/Per feeding tube x 1 dose	No additional action
3.5 – 3.6 mEq/L	20 mEq KCl PO/Per feeding tube Q2H x 2 doses	No additional action
3.3 – 3.4 mEq/L	20 mEq KCl PO/Per feeding tube Q2H x 3 doses	Recheck serum potassium level 4 hours after last oral dose
3.1 – 3.2 mEq/L	20 mEq KCl PO/Per feeding tube Q2H x 4 doses	Recheck serum potassium level 4 hours after last oral dose
< 3.1 mEq/L	20 mEq KCl PO/Per feeding tube Q2H x 4 doses	Recheck serum potassium level 4 hours after last oral dose

MAGNESIUM REPLACEMENT PROTOCOL

- Infusions should be no faster than 1gm of magnesium sulfate every 30 minutes.
- Standard Concentrations: 1 gm/100 mL and 2 gm/50 mL

Current Serum Magnesium Level	Total Magnesium Replacement	Monitoring
Serum magnesium >2.1 mg/dl	No Replacement Required	No additional action
1.8 – 2.1 mg/dl	2 grams Magnesium Sulfate IV over 2 HR	No additional action
1.3 – 1.7 mg/dl	4 grams Magnesium Sulfate IV over 4 HR	Recheck serum magnesium level 4 hours after infusion omplete
< 1.2 mg/d	6 grams Magnesium Sulfate IV over 6 HR	Recheck serum magnesium level 4 hours after infusion complete

PHOSPHORUS REPLACEMENT PROTOCOL

- Replacement must be ordered in mmol of phosphorus.
- Recommended rate = 3mmol/hr (= 4.4 mEq/h of K)
- Maximum rate = 10 mmol/hr (= 15 mEq/h of K)

Current Serum Phosphorus Level	Total Phosphorus Replacement	Monitoring
2 – 2.5 mg/dL	15 mmol Potassium Phosphate IV over 4 HR	No additional action
1 – 1.9 mg/dL	21 mmol Potassium Phosphate IV over 4 HR	Recheck serum phosphorus level 4 hours after infusion complete
< 1 mg/dL	30 mmol Potassium Phosphate IV over 4 HR *(Administered as: 15 mmol Potassium Phosphate IV Q2H x 2 doses)*	Recheck serum phosphorus level 4 hours after infusion complete
• If both potassium and phosphorus replacement required, subtract the mEq of potassium given as potassium phosphate from total amount of potassium required. (Conversion: 3 mmols KPO = 4.4 mEq K^+)		

Calcium Replacement Protocol

- For every 1 g/dL decrease of serum albumin less than 4.0 g/dL, add 0.8 mg/dL to total serum calcium level to correct value (normal serum calcium level at VUMC 8.5 - 10.5 mg/dL)
- IV replacement should be with calcium chloride (272 mg elemental calcium/1 gm

CaCl2) if a central access is present; if not, use calcium gluconate (94 mg elemental calcium/1 gm calcium gluconate)

Ionized Calcium	Total Calcium Replacement	Monitoring
0.85-0.95 mmol/L	2 g CaCl2	With next AM lab
0.75 – 0.85 mmol/L	3 g CaCl2	Recheck serum Calcium level 4 hours after infusion complete
0.65-0.75 mmol/dL	4 g Ca Cl2	Recheck serum Calcium level 4 hours after infusion complete
<0.65 mmol/L	5 g CaCl2	Recheck serum Calcium level 4 hours after infusion complete

Hyponatremia

General principles:

- Hyponatremia can be defined according to biochemical severity into
  - Mild hyponatremia: serum sodium concentration between 130 and 135 mmol/l.
  - Moderate' hyponatremia: serum sodium concentration between 125 and 129 mmol/l.
  - Profound hyponatremia: serum sodium concentration <125 mmol/l.
- Definition of hyponatremia based on time of development
  - Acute hyponatraemia: hyponatremia that is documented to exist <48 h.
  - Chronic hyponatraemia: hyponatremia that is documented to exist for at least 48 h.
  - If hyponatraemia cannot be classified, we consider it being chronic, unless there is clinical or anamnestic evidence of the contrary
- Definition of hyponatremia based on symptoms
  - Moderately symptomatic' hyponatremia: any biochemical degree of hyponatraemia in the presence of moderately severe symptoms of hyponatraemia (Table 5).
  - Severely symptomatic hyponatremia: any biochemical degree of hyponatremia in the presence of severe symptoms of hyponatremia

Table 10: Classification of symptoms of hyponatraemia

Severity	Symptom
Moderately severe	Nausea without vomiting
	Confusion
	Headache
Severe	Vomiting
	Cardiorespiratory distress
	Abnormal and deep somnolence
	Seizures
	Coma (Glasgow Coma Scale $\leq$8)

Diagnosis of hyponatremia

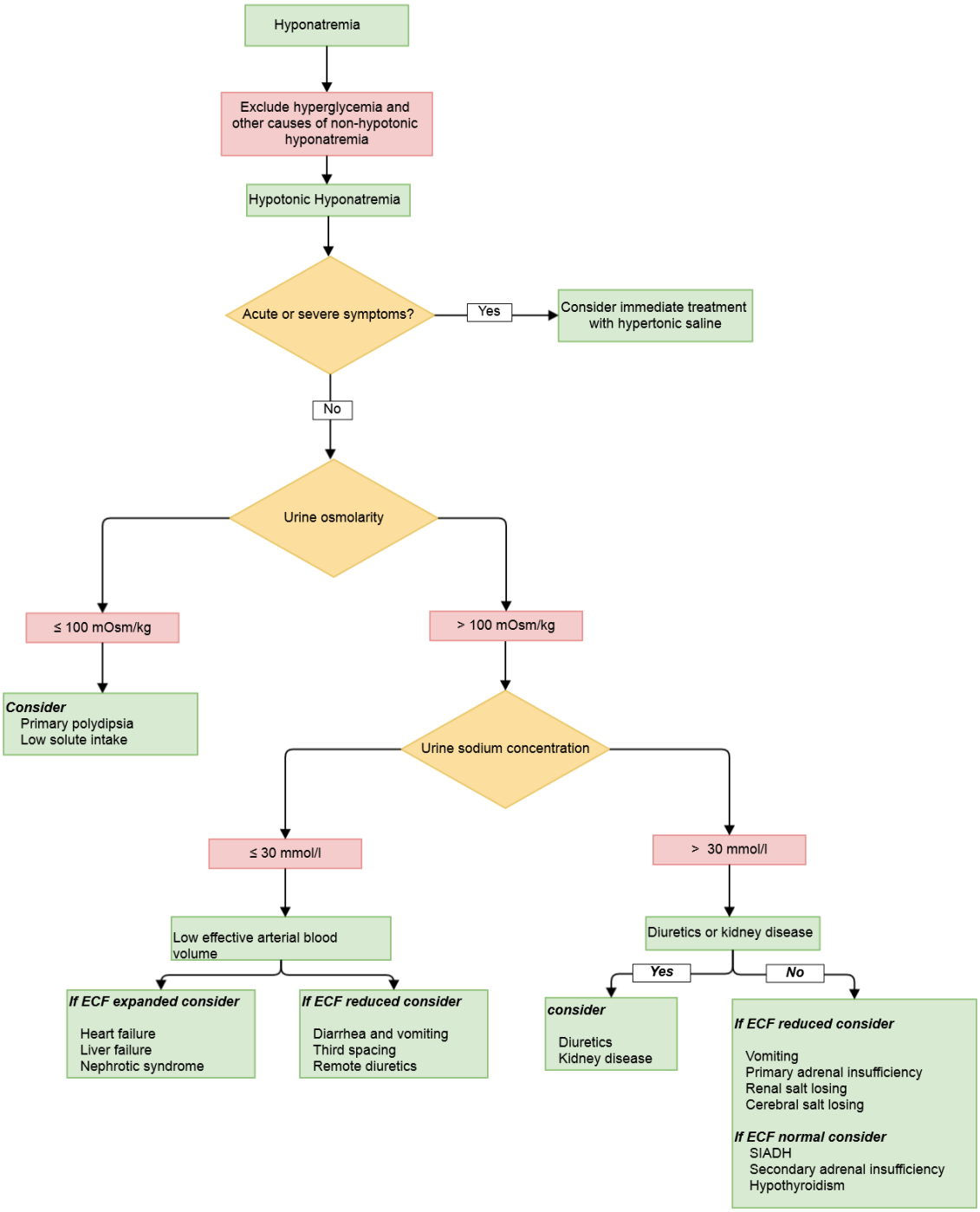

Figure 29: Diagnosis of hyponatremia

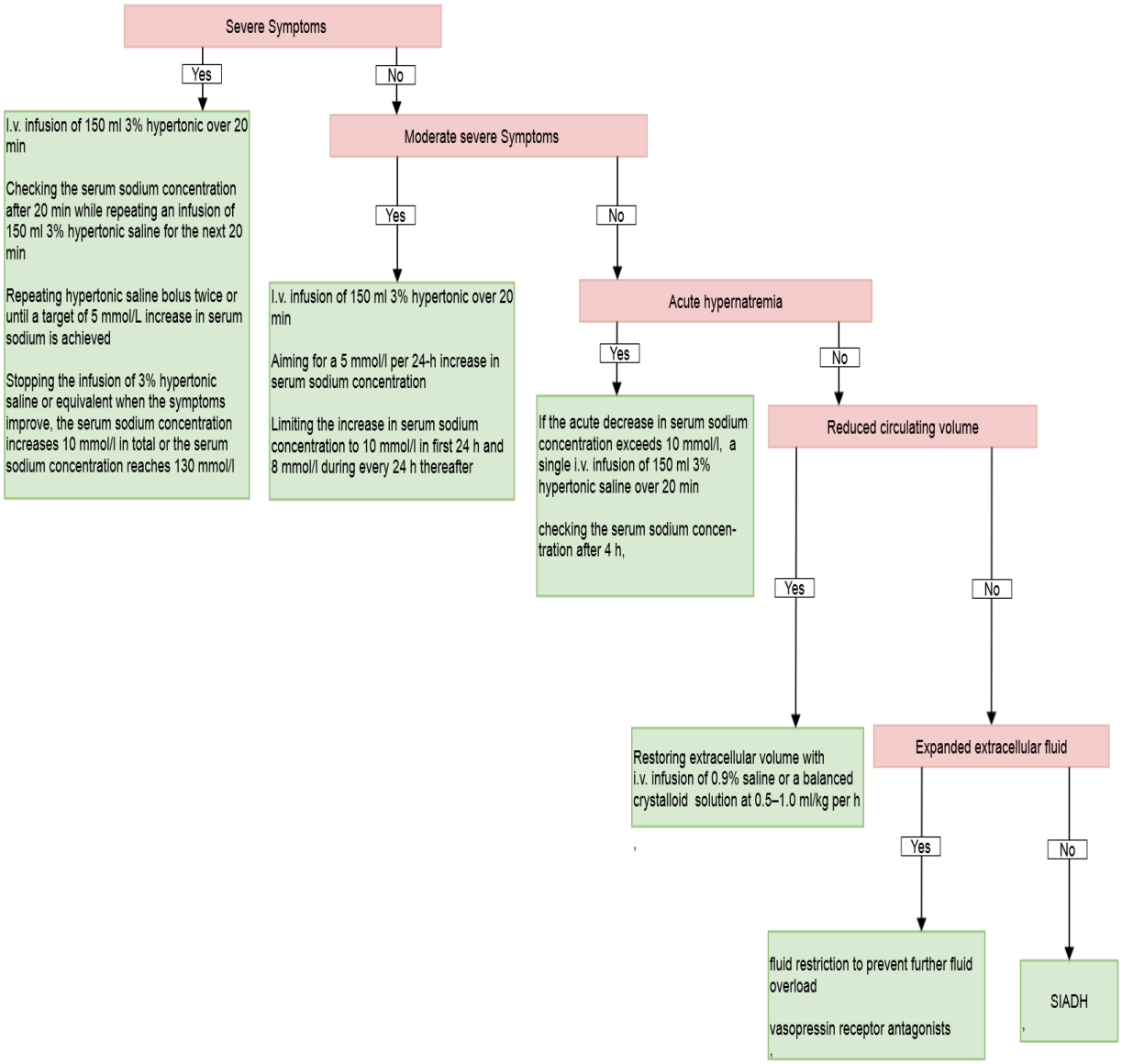

Figure 30: Management of hypotonic hyponatraemia [1]

Step 1 — **Calculate total body water in liters**

wt in kg	Men<65 yr	Men>65 or Woman<65 yr	Woman>65 yr
40	24	20	18
45	27	23	20
50	30	25	23
55	33	28	25
60	36	30	27
65	39	33	29
70	42	35	32
75	45	38	34
80	48	40	36
85	51	43	38
90	54	45	41
95	57	48	43
100	60	50	45
105	63	53	47
110	66	55	50
115	69	58	52
120	72	60	54
125	75	63	56
130	78	65	59
135	81	68	61
140	84	70	63
145	87	73	65
150	90	75	68
155	93	78	70
160	96	80	72
165	99	83	74

Step 2 — **Calculate Infusion Rate of Selected IV Fluids**

TBW (Liters)	Maximum rate of IV infusioin (ml/hr) for increase in Na of **0.5 mEq/L/hr** 0.9% Normal Saline	3% Saline	TBW (Liters)	Maximum rate of IV infusioin (ml/hr) for increase in Na of 1 **mEq/L/hr** 0.9% Normal Saline	3% Saline
20	65	19	**20**	130	39
25	81	24	**25**	162	49
30	97	29	**30**	195	58
35	114	34	**35**	227	68
40	130	39	**40**	260	78
45	146	44	**45**	292	88
50	162	49	**50**	325	97
55	179	54	**55**		107
60	195	58	**60**		117
65	211	63	**65**		127
70	227	68	**70**		136
75	244	73	**75**		147

***Note:** The infusion rates above are the *maximum* recommended rates to achieve the desired rate of Na increase. Initially, cap infusion rate of 3% saline at 75 mL/hour for a Na increase of 0.5 mEq/L/hour and at 150 mL/hr for an increase of 1 mEq/L/hour

$$\frac{\text{TBW} * (\text{goal serum Na conc} - \text{current serum Na conc}) / (\text{IV fluid Na concentration/L}) * 1000}{\text{(number of hours needed to correct Na)}}$$

Table 11: Treatment of Hyponatremia Dose Calculator

References

1. Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Eur J Endocrinol. 2014 25;170:G1-47

Burn Resuscitation

General Rules

- Acute major burns are serious life threatening conditions.
- The patient's optimal chance for survival and a meaningful recovery depends upon appropriate fluid resuscitation, airway management, and appropriate, timely burn care.

Resuscitation guidelines

- Estimate initial fluid requirements with the Parkland formula (4 mL/kg/% TBSA burned).
    - Give ½ of the fluid volume calculated over the first 8 hours from the time of the burn
    - Give the remaining half of the fluid volume over the next 16 hours.
- For ≥ 30% TBSA burns, Vitamin C infusion should be considered.
    - Ascorbic acid should be infused at 66 mg/kg/hr for the initial 24 hours of burn resuscitation.
    - The appropriate solution may be prepared by mixing 25 grams of ascorbic acid in 1000 mL of Lactated Ringer's solution (resulting in a 25 mg/mL concentration).
    - The solution bag should be covered with a black bag to prevent light-induced auto-oxidation.
    - Infusion should be begun within six hours of burn injury.
    - The fluid volume associated with the ascorbic acid infusion should be included in the total volume of fluid resuscitation calculated according to the Parkland formula.
    - Once ascorbic acid infusion is begun, point of care (POC) glucose testing results should be considered inaccurate for at least 36 hours after completing the infusion.
    - Blood glucose should be monitored using serum glucose levels whenever ascorbic acid infusions are in use.
- Avoid the use of hypertonic saline
- In patients with burns ≥ 20% TBSA:
    - Insert a central venous catheter
    - Insert a urinary (Foley) catheter
    - Monitor intra-abdominal (bladder) pressure q 4 hours during the initial resuscitation.
    - Consider invasive hemodynamic monitoring to guide resuscitation
- Resuscitation endpoints in the first 24 hours post-burn injury:
    - Monitor arterial lactate q 4 hours until < 2 mMol/L
    - Maintain urine output at 30-50 ml/hr (50-100 ml/hr if receiving Vitamin C)

- In electrical injury or rhabdomyolysis patients, serial creatinine kinase levels should be checked daily until < 2500 mcg/L
- Monitor hemoglobin to ensure that it is not trending upward

- If the patient requires ≥ 1.5 times the calculated Parkland formula volume (6 ml/kg/TBSA), consider colloid rescue:
  - 5% albumin at 1/3 Parkland rate + 2/3 Parkland rate of Lactated Ringers OR
  - 25% albumin at 1/15th the Parkland rate + 2/3 Parkland rate of Lactated Ringers.
- If the patient has received > 250 mL/kg of fluid resuscitation, intraocular pressure should be measured.

References

1. Aboelatta Y, Abdelsalam A. Volume overload of fluid resuscitation in acutely burned patients using transpulmonary thermodilution technique. J Burn Care Res. 2013;34:349-54
2. Al-Benna S. Fluid resuscitation protocols for burn patients at intensive care units of the United Kingdom and Ireland. Ger Med Sci. 2011;9:
3. Pham TN, Cancio LC, Gibran NS; American Burn Association. American Burn Association practice guidelines burn shock resuscitation. J Burn Care Res. 2008;29:257-66
4. Kahn SA, Beers RJ, Lentz CW. Resuscitation after severe burn injury using high-dose ascorbic acid: a retrospective review. J Burn Care Res. 2011;32:110-7

Stress Ulcer Prophylaxis (SUP)

General Rules

1. The goal of SUP is to prevent bleeding from gastric erosions
2. Routine prophylaxis for all patents is NOT recommended as the risk differs between patients
3. There is increasing body of evidence about the protective role of enteral feeding on gastric mucosa

Stress ulcer prophylaxis protocol

1. Start prophylaxis on patients with any of the acute risk factors below
    a. Mechanical ventilation
    b. Coagulopathy
    c. Hypoperfusion state and organ dysfunction (septic, hemorrhagic, cardiogenic shock)
    d. Severe head injury or spinal cord injury
    e. Severe burn (>35%)
    f. High dose corticosteroids (>250 hydrocortisone /day or its equivalent)
2. Consider prophylaxis for patients who are not fed and have two potential risk factor below
    a. Concomitant use of non-steroidal anti-inflammatory (NSAID) drugs
    b. Concomitant use of corticosteroids
    c. History of peptic ulcers, upper GIT disease
    d. Mild/moderate brain or spinal cord injury
3. Prophylaxis therapy of stress ulcers
    a. Use IV ranitidine 50 mg q 8 hrs. Change to oral ranitidine 150 mg q12 hrs in patients who are enterally fed.
        i. In renal failure, reduce IV dose to 50 mg q 12 hrs or oral 150 mg q 24 hrs
        ii. Proton pump inhibitors (PPIs) are indicated in patients with proven ulcers and are already on PPI treatment. PPIs are not eliminated via the renal route and dose adjustment in renal impairment is not necessary.
4. Treating active upper GI bleed in ICU
    a. PPIs remain the main stay of treatment in patients that develop active upper GI bleeding
    b. Give PPI as an infusion 8 mg/hrs over 48-72 hrs, following a loading dose of 80 mg as an adjunct to endoscopic or surgical management.
    c. For those who develop clinically significant bleed in ICU, continue PPIs for at least 2 weeks

5. Discontinuation of SUP
    a. Prophylactic therapy may be discontinued once patient is tolerating full feeds and has no more risk factors.

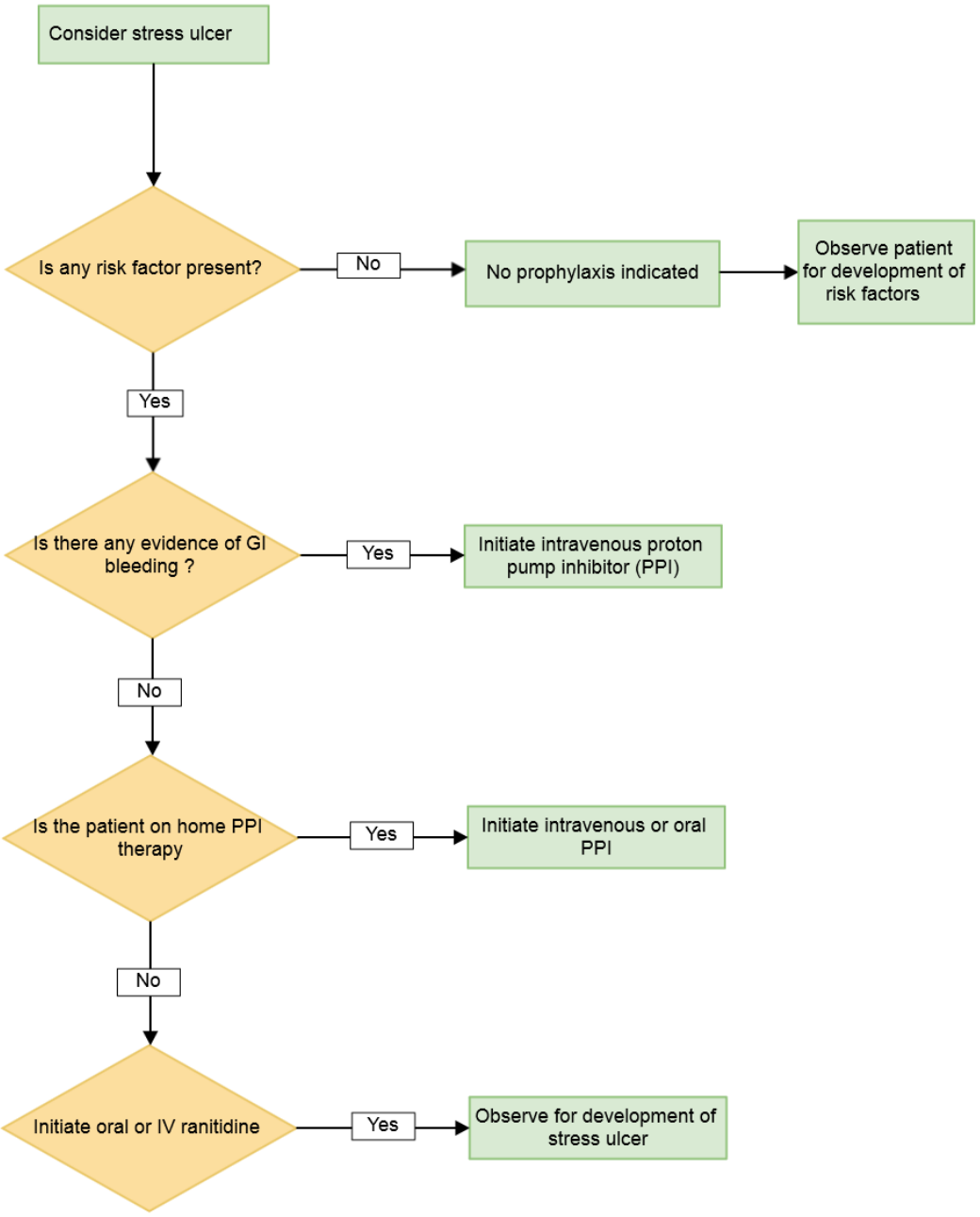

Figure 31: Stress ulcer prophylaxis protocol

References

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Gastro-intestinal hemorrhage protocol

General principles

- Gastrointestinal (GI) bleeding encompasses a wide range of diagnoses with multiple types of lesions and bleeding that can occur virtually anywhere in the GI tract
- Management and the outcome of GI bleeding depend on both the severity of the bleeding and any comorbid conditions present at the time of the bleeding
- Acute GI bleeding often requires close monitoring and management in an intensive care unit

Initial Evaluation and Resuscitation

- The first step in clinical evaluation is to assess the severity of the bleeding.
- Patients who present with hemodynamic instability and significant hematemesis will have resting tachycardia (pulse ≥ 100 per min), hypotension (systolic blood pressure <100 mmHg), or postural changes (increase in the pulse of ≥20 beats/min or a drop in systolic blood pressure of ≥ 20 mmHg on standing)
- In patients with exsanguinating bleeding or the patient who is delirious, airway should be protected by elective intubation. In conscious patients, give oxygen by nasal cannula.
- Two large-bore intravenous channels should be placed at the earliest.
- Fluid resuscitation should be started with Ringer's lactate or normal saline. Crystalloid or colloid solutions may be used for treating hypotension aiming a systolic blood pressure of more than 100 mmHg.
- Do typing and crossmatching of blood. Target hemoglobin usually around 7–8 g% for otherwise healthy individuals without active bleeding. A target hemoglobin concentration of about 9 g% would be appropriate in patients older than 65 years or those with cardiovascular disease.
- The patient should be kept nil orally. This is necessary because an urgent endoscopy or even intubation may be needed in the event of a repeat bleeding.
- Stop factors that enhance bleeding—anticoagulants (warfarin, heparin) and antiplatelet agents (aspirin, clopidogrel).

Find etiology and stratify risk

- The severity of presenting symptoms, current medications, and history are instrumental in establishing the etiology of UGI bleeding.
- The history of use of aspirin and nonsteroidal anti-in fl ammatory drugs (NSAIDs) suggests a bleeding ulcer. The history of prolonged alcohol intake and the stigmata of chronic liver disease including jaundice and ascites would indicate a possible variceal hemorrhage.

Send investigations

- Hemoglobin levels are required in all patients. It must, however, be noted that initial levels may be falsely high and underestimate true blood loss due to hemoconcentration.
- Blood should be sent urgently for cross matching and availability.
- Send blood parameters including prothrombin time, partial thromboplastin time, and platelet count.
- Blood urea, creatinine, and liver function tests may assist in diagnosing the cause and severity of bleeding.

General treatment

- Any coagulopathy found needs to be corrected by appropriate blood products. If prothrombin time/international normalized ratio is prolonged, give fresh frozen plasma or vitamin K injection.
- Proton-pump inhibitors: 80 mg IV bolus should be administered followed by intravenous infusion of 8 mg/h or 40 mg 12 hourly
- If there is known or suspected variceal bleeding (or known or suspected chronic liver disease), empiric treatment with terlipressin 2 mg IV stat followed by 2 mg IV QDS and a dose of broad-spectrum antibiotics should be given.
- If there is history of active alcohol abuse, thiamine replacement should be started.
- Insert the nasogastric tube
    - The nasogastric tube insertion is helpful in many ways. The type of aspirate such as fresh blood, bilious, or altered blood helps in determining whether bleeding is ongoing or has stopped.
    - Gastric lavage before endoscopy also helps in giving a clear view for endoscopy.
- Carry out endoscopy
    - Endoscopy is a mainstay for all cases of UGI bleeding. It enables Identification of the source of bleeding.

      Timing of endoscopy: After resuscitation, an endoscopy is arranged. Patients with profuse hemorrhage may need emergency endoscopy; the endoscopy should take place within 24 h of presentation, both to guide management and to facilitate the early discharge of patients with a low risk of recurrent bleeding.

Specific treatment

A. For nonvariceal bleeding

- Intravenous proton-pump inhibitor bolus is followed by infusion for 72 h after endoscopic hemostasis; oral proton-pump inhibitors can be started after completion of intravenous therapy.
- Stop NSAIDs and substitute with less toxic drugs. There is no role for H2 blocker, somatostatin, or octreotide. Oral intake of clear liquids can be initiated 6 h after endoscopy in patients with hemodynamic stability.
- Surgical or interventional radiologic consultation should be taken for angiography for selected patients with failure of endoscopic hemostasis or massive rebleeding.

B. For variceal bleeding

- Vasoactive drug treatment should be continued (terlipressin for 48 h, octreotide, or somatostatin each for 3 days).
- Antibiotic therapy should be commenced/continued.
- Balloon tamponade should be considered as a temporary salvage treatment for uncontrolled bleeding.
- Transjugular intrahepatic portosystemic stent shunting is recommended as the treatment of choice for uncontrolled variceal hemorrhage.

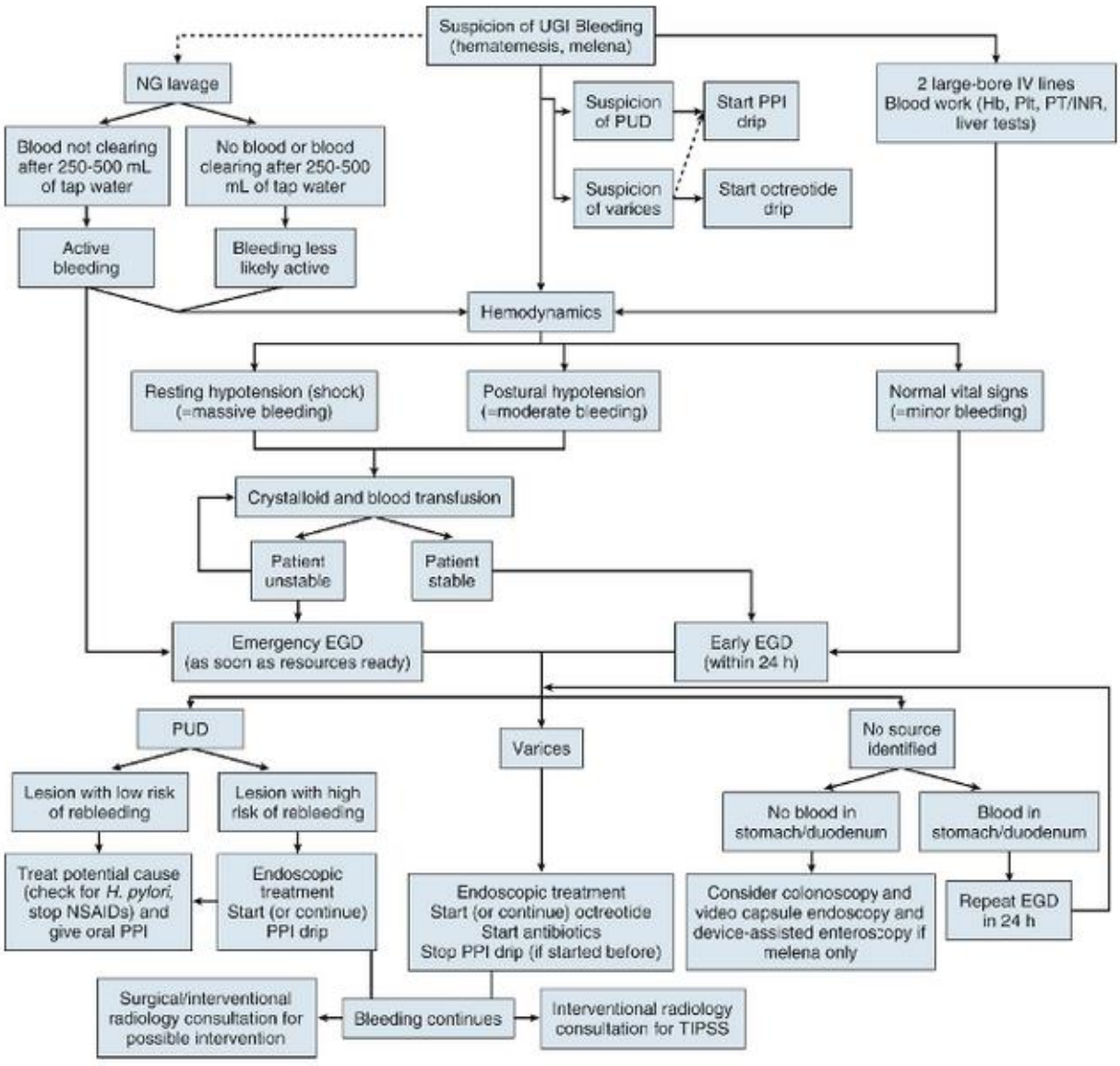

Figure 32: Approach to managing upper gastrointestinal bleeding in critical care patients.

References

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Management of DKA

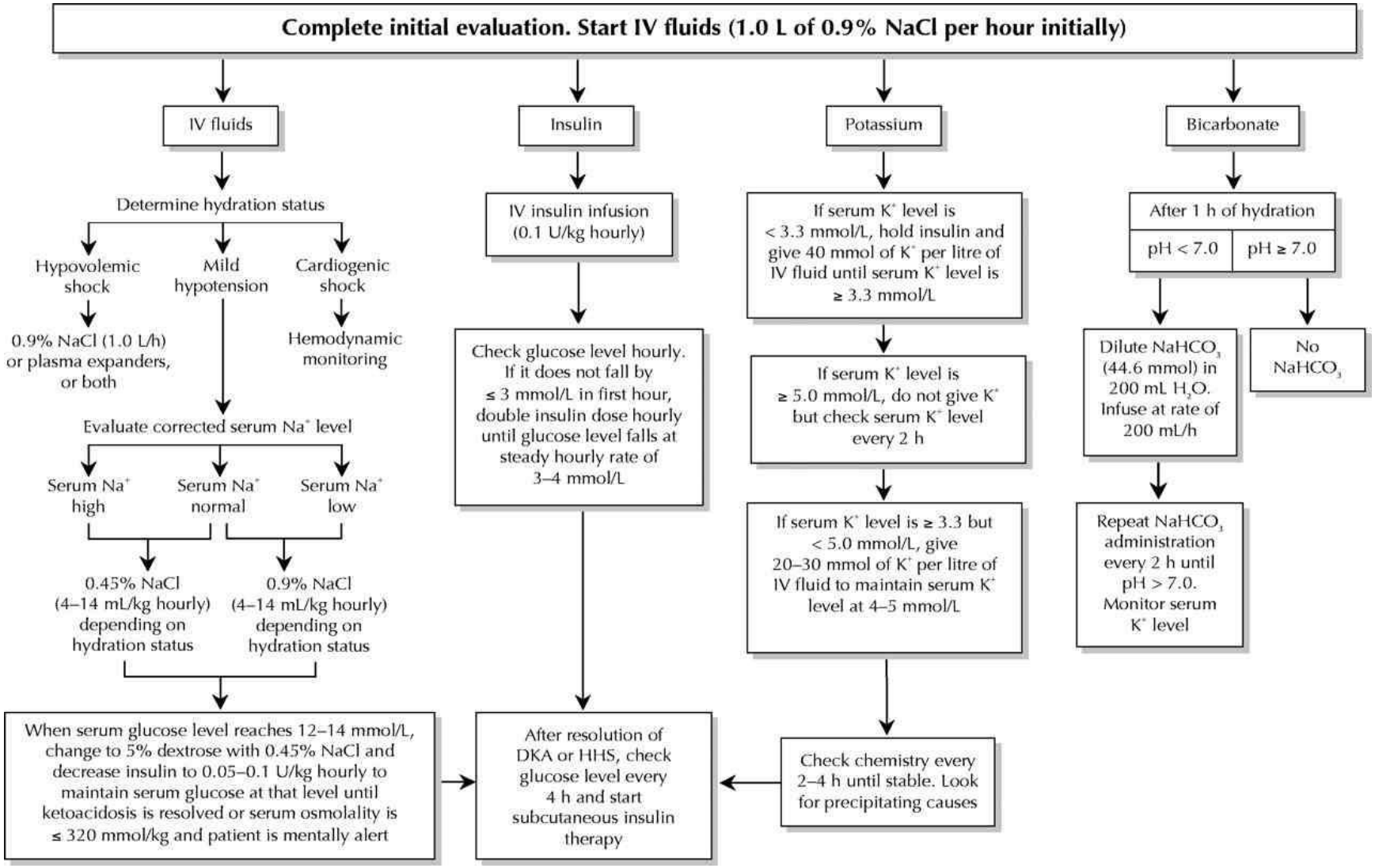
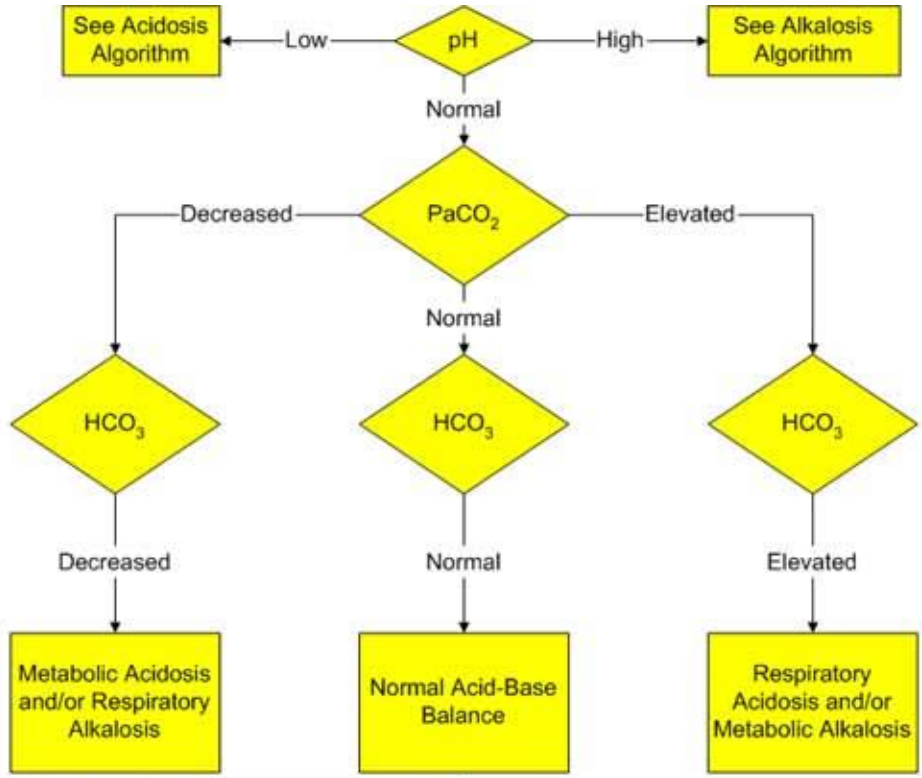


Figure 33: Management of DKA

Acid-Base protocol



Normal pH: 7.35-7.45
Acidemia: pH < 7.35
Alkalemia: pH > 7.45
Normal $PaCO_2$: 35-45 mm Hg
Normal HCO_3:22-26 meq/L
Anion Gap: Na - (Cl + HCO_3)
Normal Anion Gap: 8-12
Excess AG = Observed AG - Normal AG
Delta HCO_3 = Normal HCO_3 - Measured HCO_3

Diagnosis of Triple Acid-Base Disorders:

Rule 1: Triple acid-base disorders involve metabolic acidosis and metabolic alkalosis with one primary respiratory disorder. Respiratory acidosis and respiratory alkalosis can not co-exist.

Rule 2: For high anion gap acidosis, the serum HCO_3 will fall by 1 meq/L for each meq increase in anion gap. This relationship helps make diagnosis of mixed metabolic acidosis and alkalosis:

Calculate Delta Anion gap

Calculate Delta HCO_3

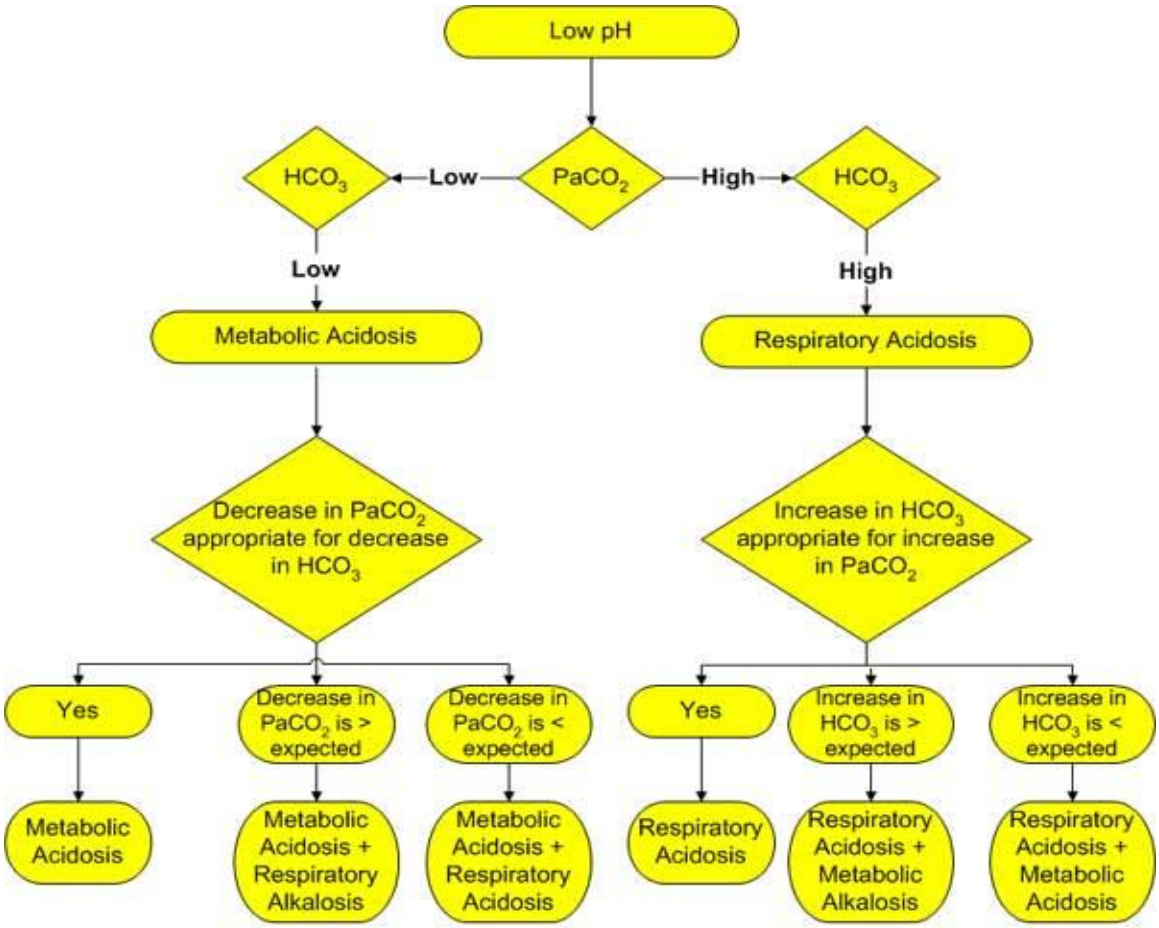
If Excess AG is > Delta HCO_3: Patient has superimposed metabolic alkalosis in addition to primary high AG metabolic acidosis

If Excess AG is < Delta HCO_3, suspect a combined high AG acidosis plus normal AG acidosis.

Rule 3: If AG is > 35, suspect a combined metabolic acidosis plus metabolic alkalosis.

Rule 4: In a patient with metabolic acidosis, if excess AG + Measure HCO_3 is > 30, there is underlying metabolic alkalosis; if < 23, there is associated non AG acidosis.

Acidosis



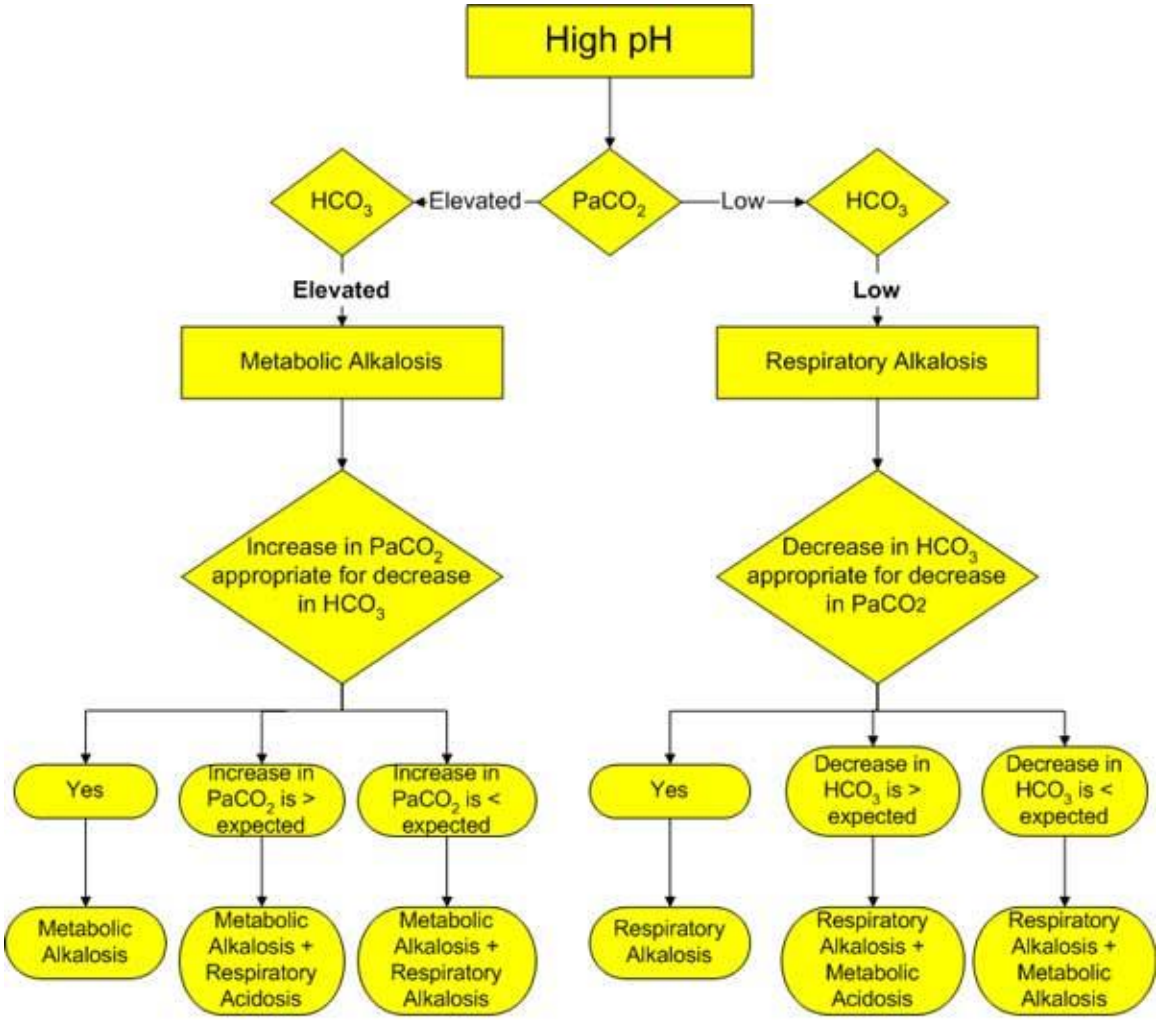
Compensation for Metabolic Acidosis

For each meq/L decrease in HCO_3, $PaCO_2$ decreases by 1.2
Expected $PaCO_2$ = 1.5 x HCO_3 + 8 (+/- 2)
$PaCO_2$ = Last 2 digits of pH

Compensation for Respiratory Acidosis

Acute: For every 10 mmHg increase in $PaCO_2$, HCO_3 increases by 1 meq/L
Chronic: For every 10 mmHg increase in $PaCO_2$, HCO_3 increase by 3.5 meq/L

Alkalosis



Compensation for Metabolic Alkalosis

For each meq/L increase in HCO_3, $PaCO_2$ increases by 0.6 mm Hg

Compensation for Respiratory Alkalosis

Acute: For every 10 mm decrease in $PaCO_2$, HCO_3 decreases by 2 meq/L
Chronic: For every 10 mm decrease in $PaCO_2$, HCO_3 decrease by 4-5 meq/L

References

Kellum JA (2005) Disturbances of acid–base balance. Textbook of Critical Care, 5th edn, eds. Fink MP Abraham B, Vincent JL, Kochanek PM. Philadelphia, PA: Elservier.

Transfusion and Coagulopathy Management protocol

Management of anemia and red cell transfusion

General Principle:

- Anemia is highly prevalent among the critically ill; 60% of patients admitted to intensive care units (ICU) are anaemic and 20–30% have a first haemoglobin concentration (Hb) <9.0 g/dL
- After 7 d, 80% of ICU patients have an Hb <9.0 g/dL and 30–50% of ICU patients receive red cell (RBC) transfusions.

Protocol of red blood cell transfusion

- A transfusion threshold of 7.0 g/dL or below, with a target Hb range of 7.0–9.0 g/dL, should be the default for all critically ill patients, unless specific co-morbidities or acute illness-related factors modify clinical decision-making.
- Transfusion triggers should not exceed 9.0 g/dL in most critically ill patients.
- Erythropoietin should NOT be used to treat anemia in critically ill patients.
- In the absence of clear evidence of iron deficiency, routine iron supplementation is NOT recommended during critical illness.
- Red cell transfusion transfusion should NOT be used as a strategy to assist weaning from mechanical ventilation when the Hb is >7.0 g/dL

Transfusion in patient with sepsis

- In the early resuscitation of patients with severe sepsis, if there is clear evidence of inadequate DO_2, transfusion of RBCs to a target Hb of 9.0–10.0 g/dL should be considered.
- During the later stages of severe sepsis, a restrictive approach to transfusion should be followed with a target Hb of 7.0–9.0 g/dL

Transfusion in neurocritical care

- In patients with severe TBI (GCS ≤ 8): Target haemoglobin level ≥ 10 g/dL
- In patients with subaracnoid hemorrhage, the target Hb should be 8.0–10.0 g/dL

- In patients presenting to the ICU with an acute ischemic stroke the Hb should be maintained above 9.0 g/dL

Transfusion in patient with ischemic heart disease

- In patients suffering from ACS the Hb should be maintained at >8.0 g/dL

Transfusion related acute lung injury (TRALI) & Transfusion associated circulatory overload (TACO)

- Patients developing acute dyspnoea with hypoxia and bilateral pulmonary infiltrates during or within 6 h of transfusion should be carefully assessed for the probability of TRALI and patients should be admitted to a critical care area for supportive treatment and monitoring

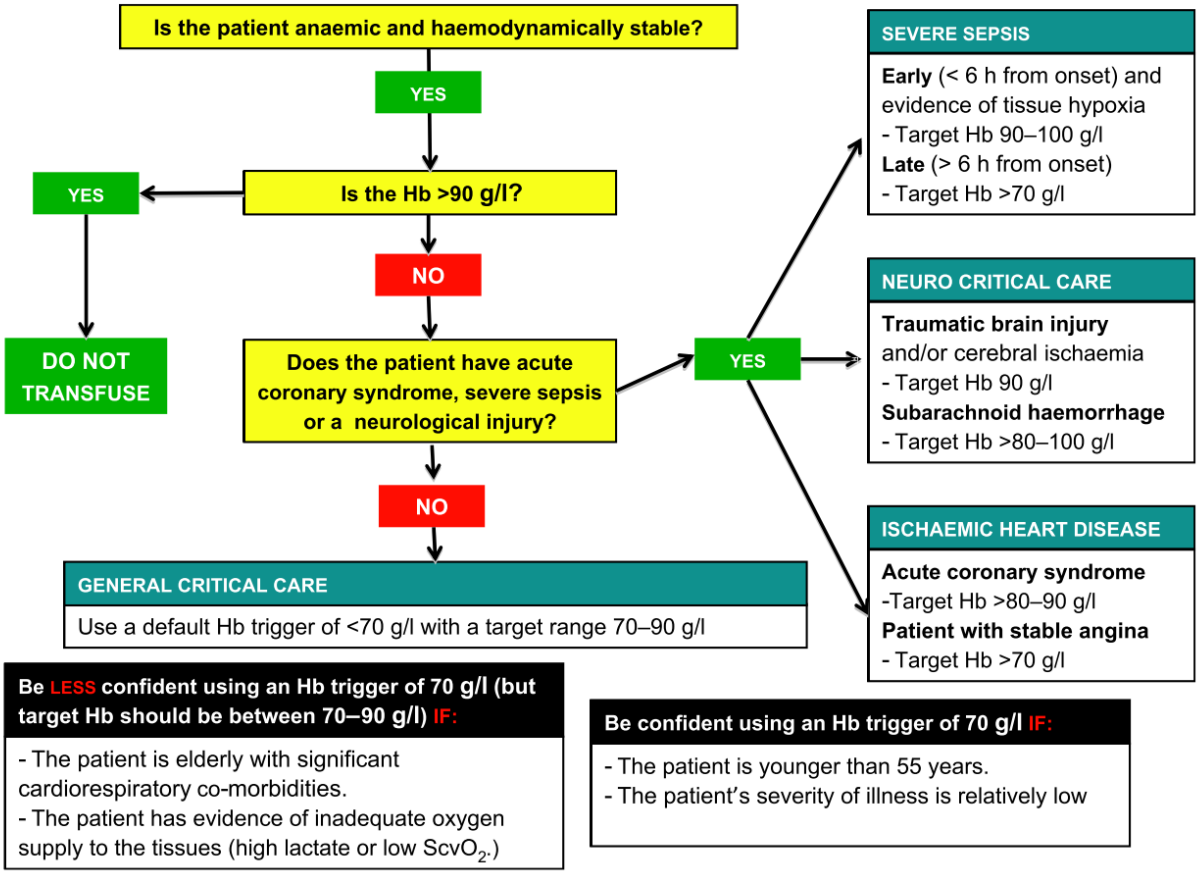


Figure 34: A suggested approach to transfusion in critical care

References

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Management of coagulopathy

Protocol of Fresh frozen plasma (FFP)transfusion

- Reversal of warfarin effect: FFP should only be used for the reversal of warfarin anticoagulation in the presence of major bleeding.
- Perioperative transfusion in the presence of major bleeding
- Disseminated intravascular coagulopathy: consider FFP if there clinical evidence of bleeding

Protocol of Platelet transfusion

Indication	Transfusion trigger
• Prophylactic use pre-procedure ○ Surgery involving critical sites (brain-eye) ○ Non critical site surgery (laparotomy) ○ Neuraxial blockade	 100.000 50.000 75.000
• Routine prophylactic use to reduce bleeding	10.000
• Prophylactic use in patients with additional risk factors e.g. sepsis	10.000-20.000

Disseminated intravascular coagulopathy

General principle:

- Bleeding manifestation due to disseminated intravascular coagulation (DIC) occurs in 1% of hospital admission.

Management:

I. Establish diagnosis

1. Take history of known systemic conditions associated with DIC and coagulation disorders
2. Laboratory investigations:
    a. Complete blood count
    b. Prothrombin time (PT), partial thromboplastin time (PTT), INR
    c. Fibrinogen level, fibrin degradation product (FDP), D-dimer.
    d. Renal and liver function tests.
    The commonest abnormality is thrombocytopenia followed by elevated FDPs, prolonged PT, prolonged PTT, and a low fibrinogen.
3. Calculate DIC score of International Society of Thrombosis and Hemostasis (ISTH).
    a. More than 5 overt DIC: repeat score daily.
    b. Less than 5 suggestive for nonovert DIC: repeat for the next 1–2 days.

Table: ISTH diagnostic score of DIC

Platelet count		
	>100.000	0
	50000-100000	1
	>100000	2
Fibrin marker		
	No increase	0
	Moderate increase	2
	Strong increase	3
Prolonged PT		
	< 3 s	0
	> 3 but < 6 s	1
	>6 s	2
Fibrinogen level		
	≥1 g/dL	0
	< 1 g/dL	1

II. Management

- Treatment of underlying cause.
- Transfusion of platelets or plasma (components) in patients with DIC should not primarily be based on laboratory results and should in general be reserved for patients that present with bleeding.
- In patients with DIC and bleeding or at high risk of bleeding (e.g. postoperative patients or patients due to undergo an invasive procedure) a platelet count should be maintained more than 50,000
- In non-bleeding patients with DIC, prophylactic platelet transfusion is not given unless it is less than 10,000.
- In bleeding patients with DIC and prolonged PT and PTT FFP should be administered at dose 15-30 ml/kg
- Severe hypofibrinogenemia (<100 mg/dL) may be treated with fibrinogen concentrate or cryoprecipitate.
- In cases of DIC where thrombosis predominates, weight adjusted doses (e.g. 10 µ/kg/h) may be used.
- Do not use antifibrinolytic agents as they may aggravate thrombosis.

References

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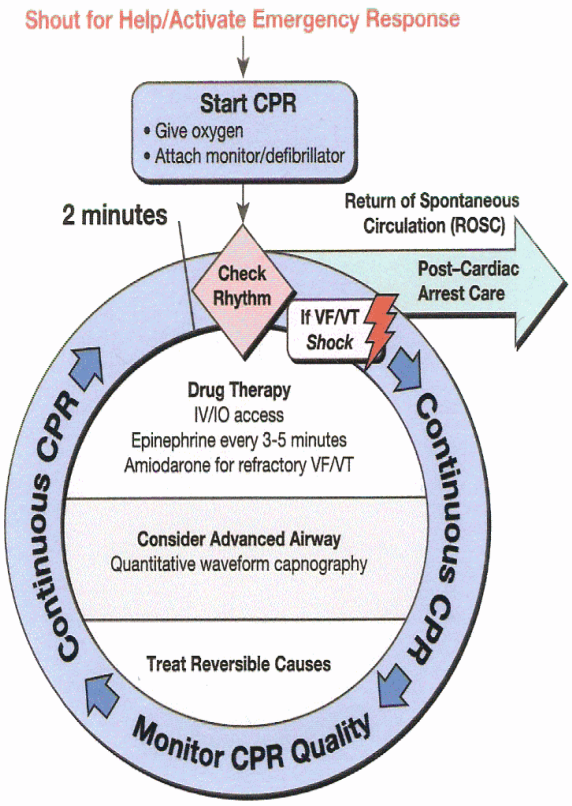
Cardiopulmonary resuscitation

Figure 4
Circular ACLS Algorithm



CPR Quality
- Push hard (≥2 inches [5 cm]) and fast (≥100/min) and allow complete chest recoil
- Minimize interruptions in compressions
- Avoid excessive ventilation
- Rotate compressor every 2 minutes
- If no advanced airway, 30:2 compression-ventilation ratio
- Quantitative waveform capnography
  - If P_{ETCO_2} <10 mm Hg, attempt to improve CPR quality
- Intra-arterial pressure
  - If relaxation phase (diastolic) pressure <20 mm Hg, attempt to improve CPR quality

Return of Spontaneous Circulation (ROSC)
- Pulse and blood pressure
- Abrupt sustained increase in P_{ETCO_2} (typically ≥40 mm Hg)
- Spontaneous arterial pressure waves with intra-arterial monitoring

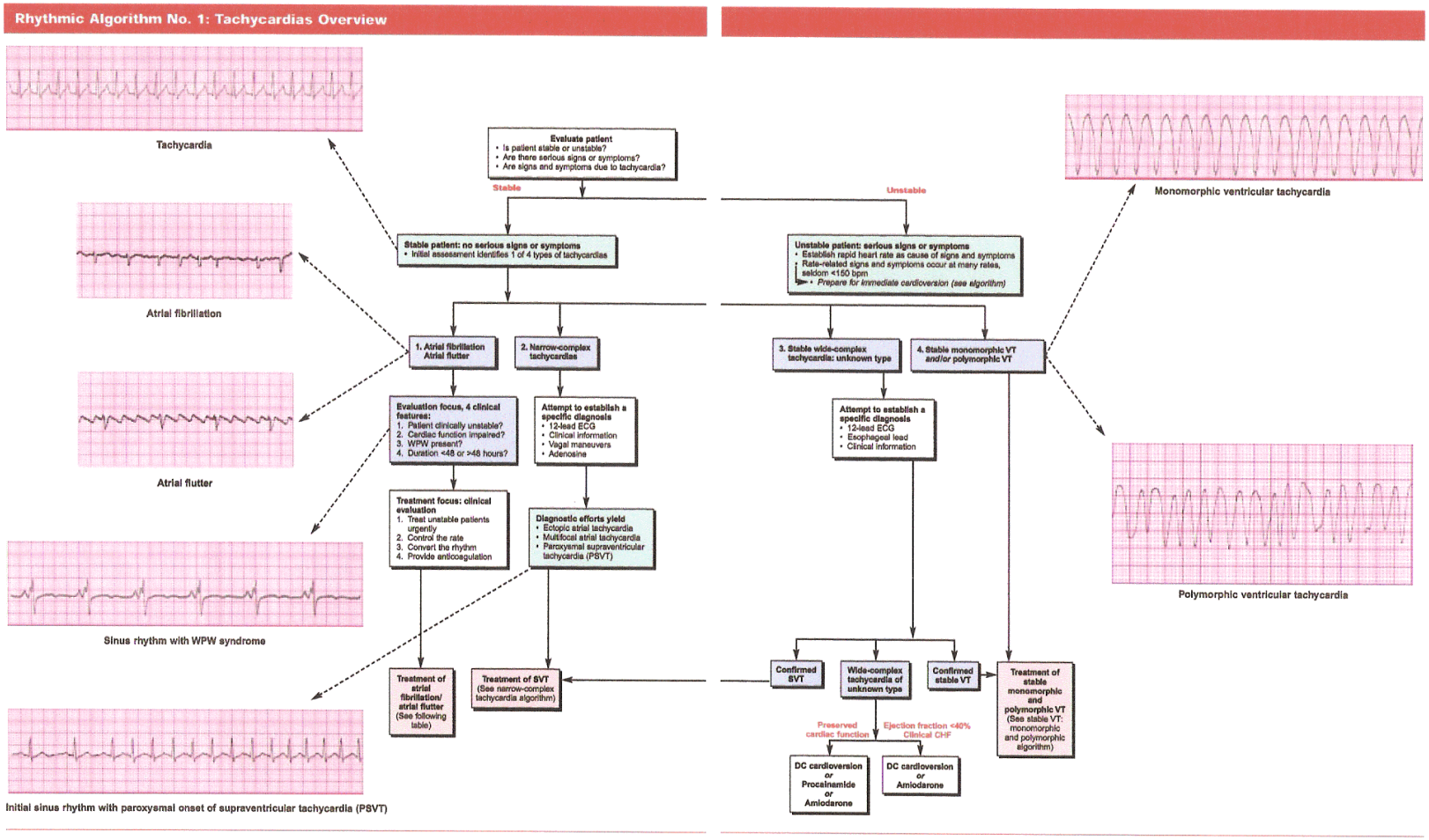
Shock Energy
- **Biphasic:** Manufacturer recommendation (120-200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered.
- **Monophasic:** 360 J

Drug Therapy
- **Epinephrine IV/IO Dose:** 1 mg every 3-5 minutes
- **Vasopressin IV/IO Dose:** 40 units can replace first or second dose of epinephrine
- **Amiodarone IV/IO Dose:** First dose: 300 mg bolus. Second dose: 150 mg.

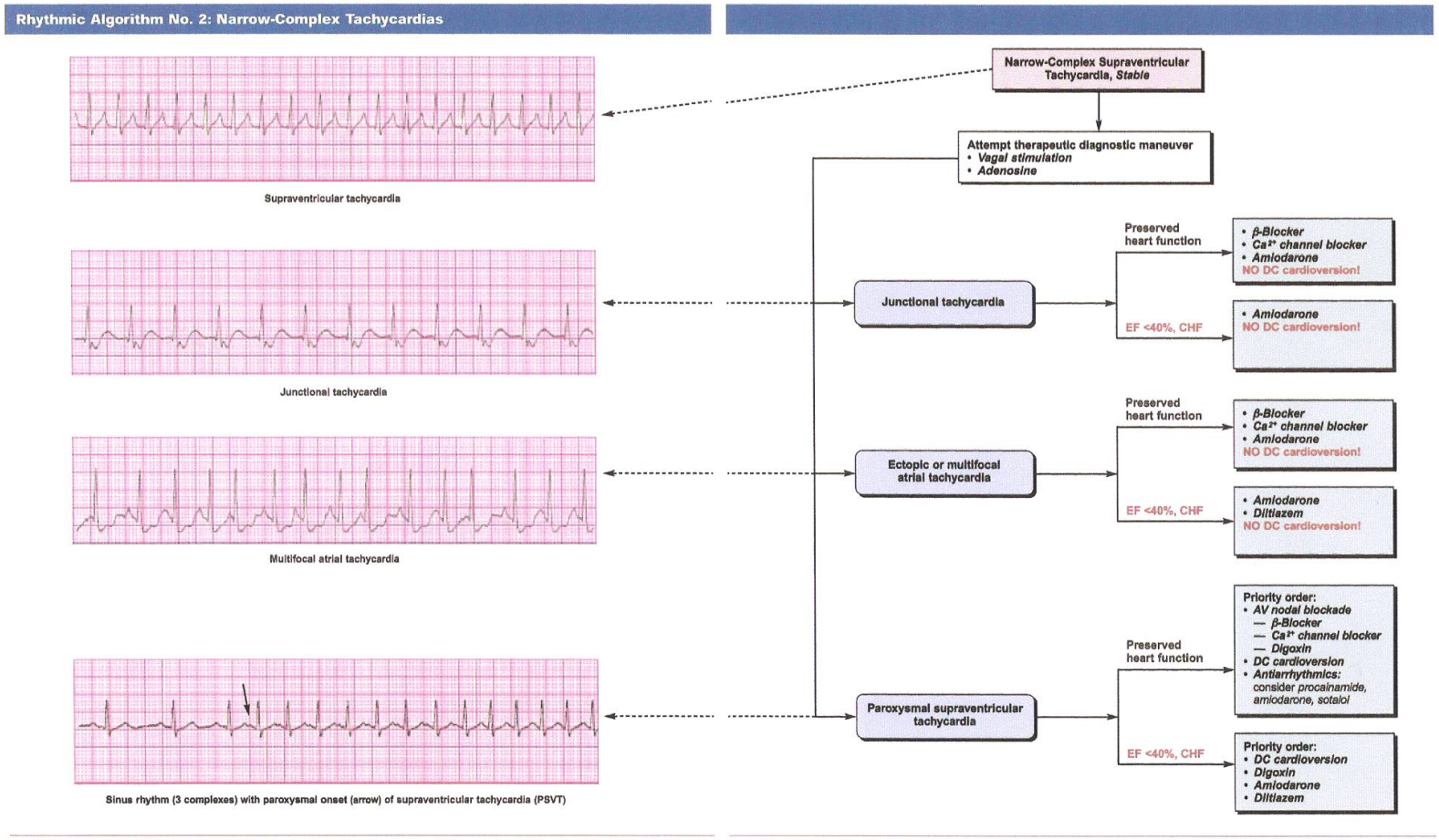
Advanced Airway
- Supraglottic advanced airway or endotracheal intubation
- Waveform capnography to confirm and monitor ET tube placement
- 8-10 breaths per minute with continuous chest compressions

Reversible Causes
- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hypo-/hyperkalemia
- Hypothermia
- Tension pneumothorax
- Tamponade, cardiac
- Toxins
- Thrombosis, pulmonary
- Thrombosis, coronary

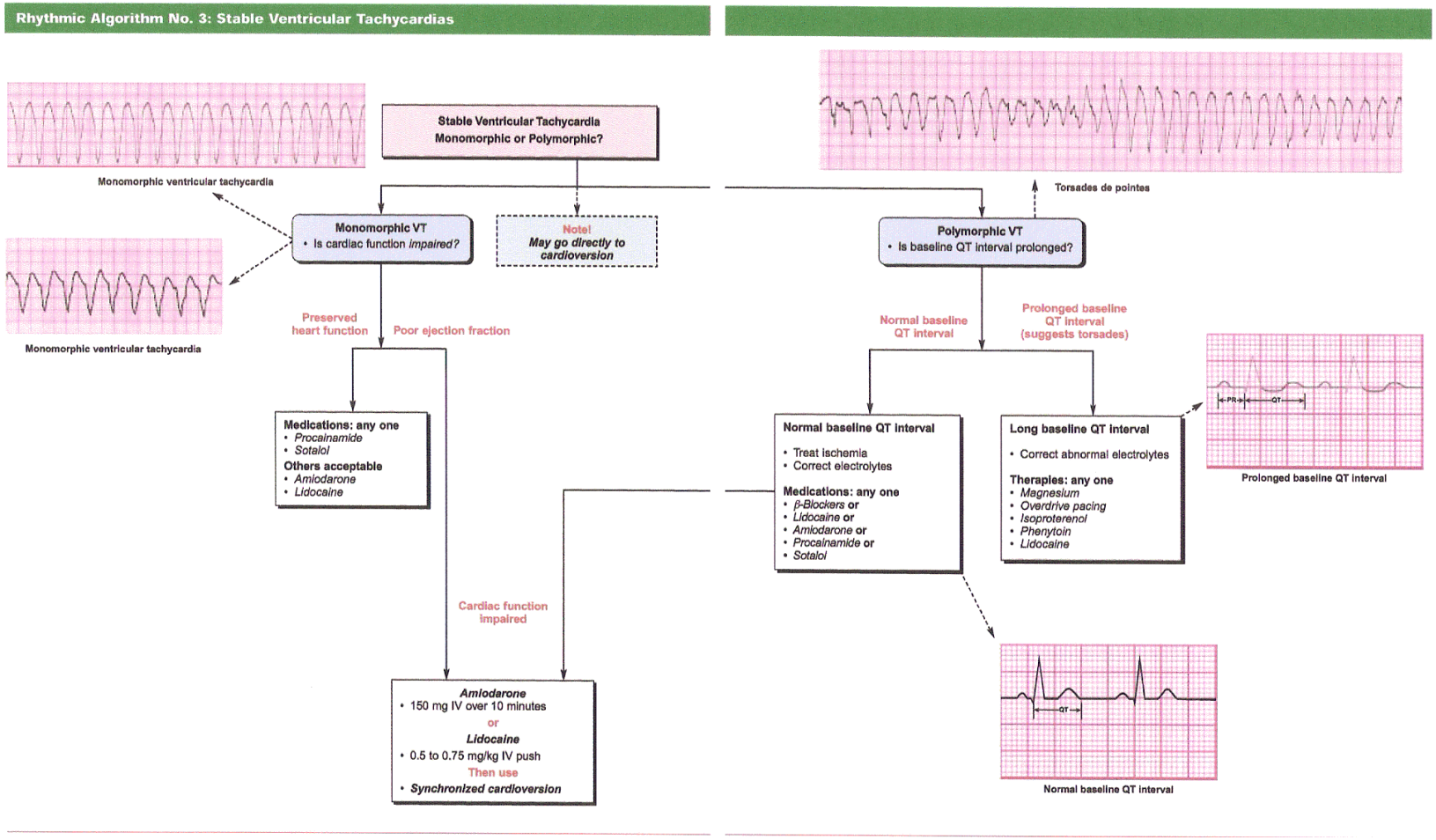
ACLS guideline of Tachy-arrhythmia



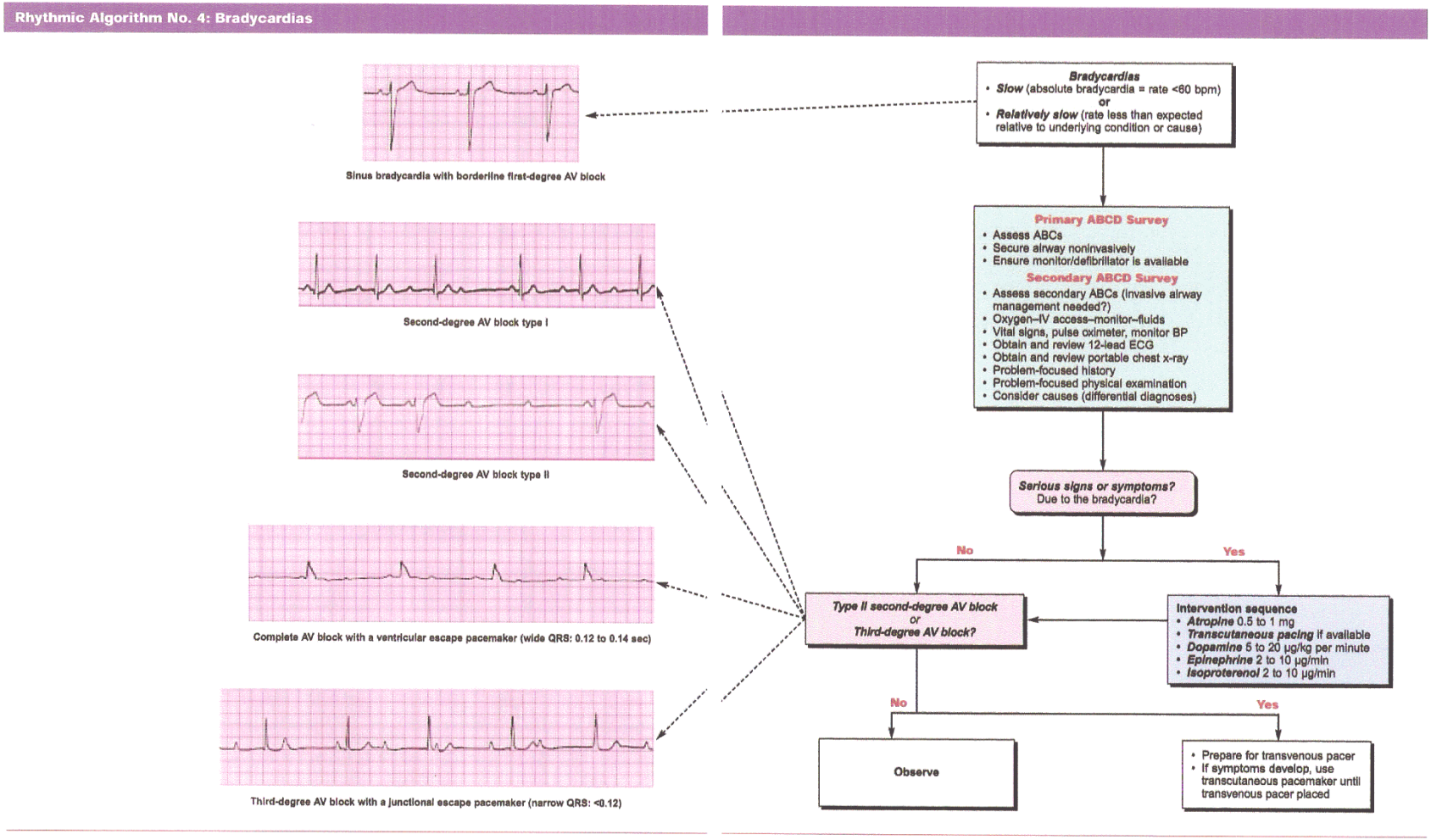
ACLS guideline of Narrow-Complex Tachycardias



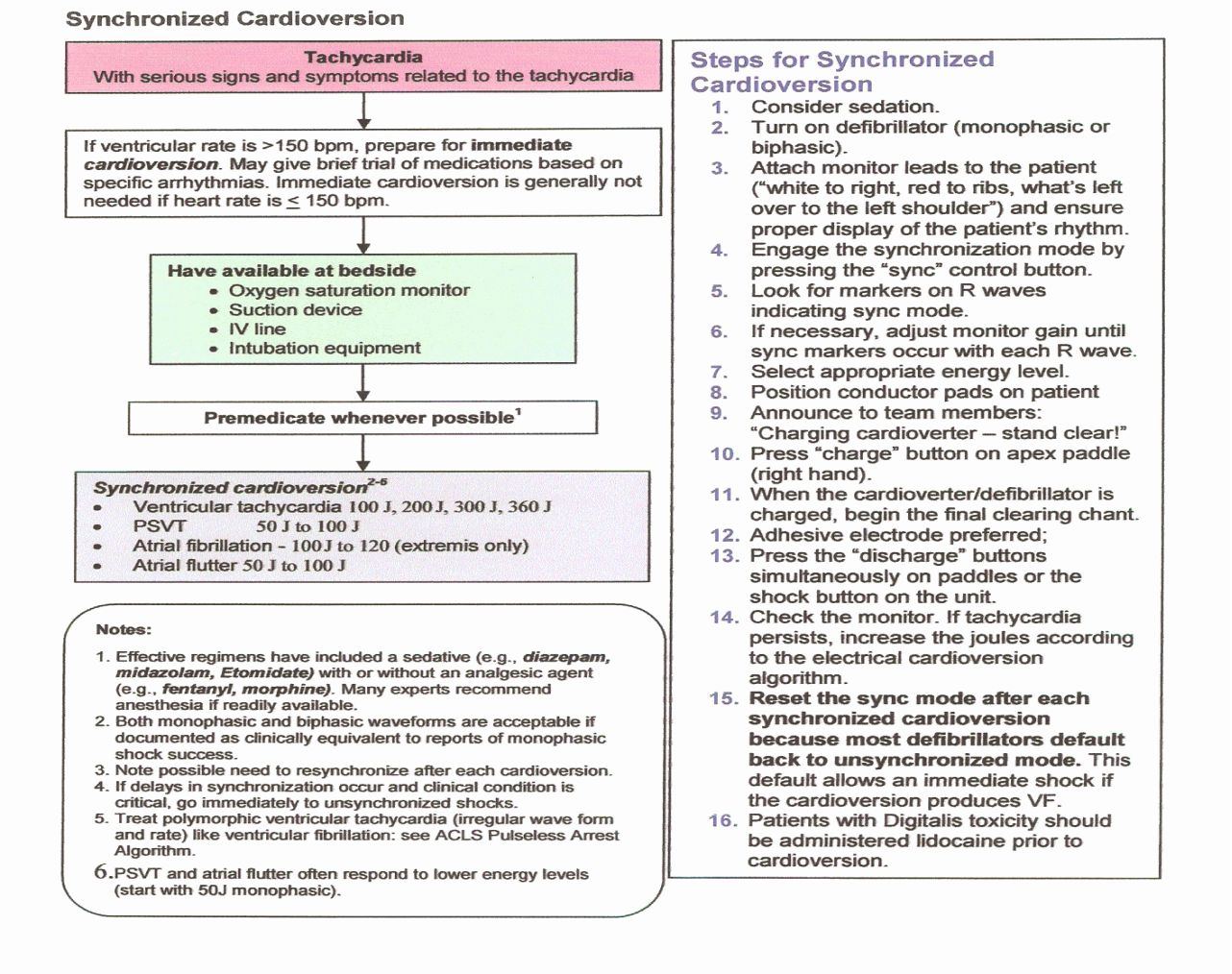
ACLS guideline of stable Ventricular Tachycaridas



ACLS guideline of Bradycardia



Electric cardioversion



Energy level of cardioversion

	Monophasic				ZOLL Biphasic				
Defibrillation	200J	300J	360J	360J	120J	150J	200J	200J	
Synchronized Cardioversion	100J	200J	300J	360J	75J** 70J*	120J	150J	200J	
Pediatric Defibrillation	2J/kg				2J/kg				
Internal Defibrillation	Maximum of 50J				5J	10J	20J	30J	50J

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Post-Return of Spontaneous Circulation (ROSC)

Procedures

Ventilation

- Place patient on AC Mode
- Set Vt to 8 ml/kg Ideal Body Weight
- Set IFR to 60 lpm
- Set Initial rate to 18 bpm
- Set Initial O2 to 50%
- Titrate FiO2/PEEP to achieve ABG Saturation 94-96%.
- Often pulse ox will not read well due to peripheral vasoconstriction

Hemodynamic Goals

Ensure Adequate Preload

- Assess by passive leg raise, pulse pressure variation. CVP may provide some indication if very low.
- Use normal saline, or lactated ringers. Use room temperature fluid if patient at goal temperature.
- Replace patient's urine losses 1:1

MAP > 65

- at all times, MAP > 80 is preferred to augment cerebral perfusion
- Preferred initial pressor is norepinephrine, may add epinephrine if necessary
- If MAP is < 80 and CVP > 10 perform passive straight leg raise to assess fluid responsiveness.
- If MAP > 100, start nitroglycerin infusion

Corrected ScvO2 > 70

- If ScvO2 < 70 and HB < 7.0 g/dL (some would advocate <10 as trigger), transfuse patient
- If HB ≥ 7.0 g/dL, evaluate echocardiogram and consider inotropes vs. balloon pump/revascularization

Lactate

- Hypothermia will raise lactate levels and post-arrest patients will have high lactate.
- Send a baseline level after the patient achieves goal temperature.
- From this point on, the lactate should stay the same or drop.
- If lactate is increasing, the patient is under-resuscitated or seizing

Sedation & Pain Control

- To gain the full benefits of hypothermia, it is imperative that the patient is adequately sedated
- Optimize fentanyl infusion rate first
- Add on propofol or midazolam if necessary
- Titrate to Ramsay Score of 4/5

Lab & Electrolyte

- Send ABG with Electrolytes and Lactate Q 2 hour for first 4 hours, then Q 4 hours.
- On arrival, send CMP, CBC, Lytes, PT/PTT, Lipase, Cardiac Enzymes, Type and Hold, & Pan-Cultures.
- Send CMP (complete metabolic panel) and CBC Q 12 hours.
- Send Cardiac Enzymes Q 12 hours.
- Keep Magnesium at high-normal at all times with aggressive IV repletion
- Replete Potassium if < 3.8 with IV KCl
- Keep iCal at high normal at all times
- Keep Sodium at least 140 at all times, 150 is preferable
- Keep Glucose < 150 with Insulin Drip (preferred) or Subcutaneous Regular Insulin

DVT Prophylaxis

- If no contraindication, Heparin 5000 units subcutaneous Q 8 hours

Stress Ulcer Prophylaxis

- PPI 40 mg IV x 1

VAP Prophylaxis

- VAP bundle

Induced Hypothermia Protocol

Inclusion Criteria (Must have All)

- Post Cardiac Arrest (Any rhythm as cause of arrest is eligible)
- ROSC < 30 min from EMS/Code Team Arrival
- Time now <6 hrs from ROSC
- Comatose (Does not follow commands)
- MAP > 65 on no more than one vasopressor

Exclusion Criteria

- Patient has poor baseline status, or terminal disease
- Active or Intracranial Bleeding

- Traumatic etiology for arrest
- Pregnancy (Relative-Consider OB/Gyn consult)
- Recent Major Surgery (Relative)
- Severe Sepsis/Septic Shock as cause of Arrest (Relative)

Protocol

- Send blood for: CMP, LFTs, Superstat I, Lactate, CBC, PT/PTT, CK/MB/Troponin, Lipase/Amylase
- Completely expose patient and place cooling blanket above and below with nothing between blanket & skin.
- Place temp probe in mid-esophagus (~4 cm above xiphoid via oral/nasal); if unable to place in esophagus, probe can be placed rectally (5 cm)
- List time Now (Starting Protocol): List Initial Patient Temperature: ° C
- If initial temperature is < 33º C, allow patient to warm to 33º C.
- Begin opioids & sedation protocol. Titrate to Ramsay Score 4/5
- Infuse refrigerated crystalloid, preferably through large bore, peripheral IV Administer at ~100 ml per minute using pressure bag (evacuate air first). Maximum initial infusion is 30 cc/kg; if patient not < 34º C after this amount, wait 15 minutes before giving further 250 cc boluses Q 10 minutes.
- Administer IV perfalgan 1 gm / 6 hours or paracetamol GI 500 mg Q6
- If during induction, pt has shivering unrelieved by the above meds, Vecuronium 0.1 mg/kg x1 can be used
- If patient's temperature rises above 34º C, infuse 250 cc boluses of cold crystalloid Q 10 min until <34º C
- Maintain temperature 32-34º C for 24 hours (ideal temperature is 33º C).
- Significant bleeding or severe hemodynamic instability, consider rewarming
- Maintain MAP>80: Multiple Pressors and/or Dobutamine may be used during protocol, if fluid loading ineffective.

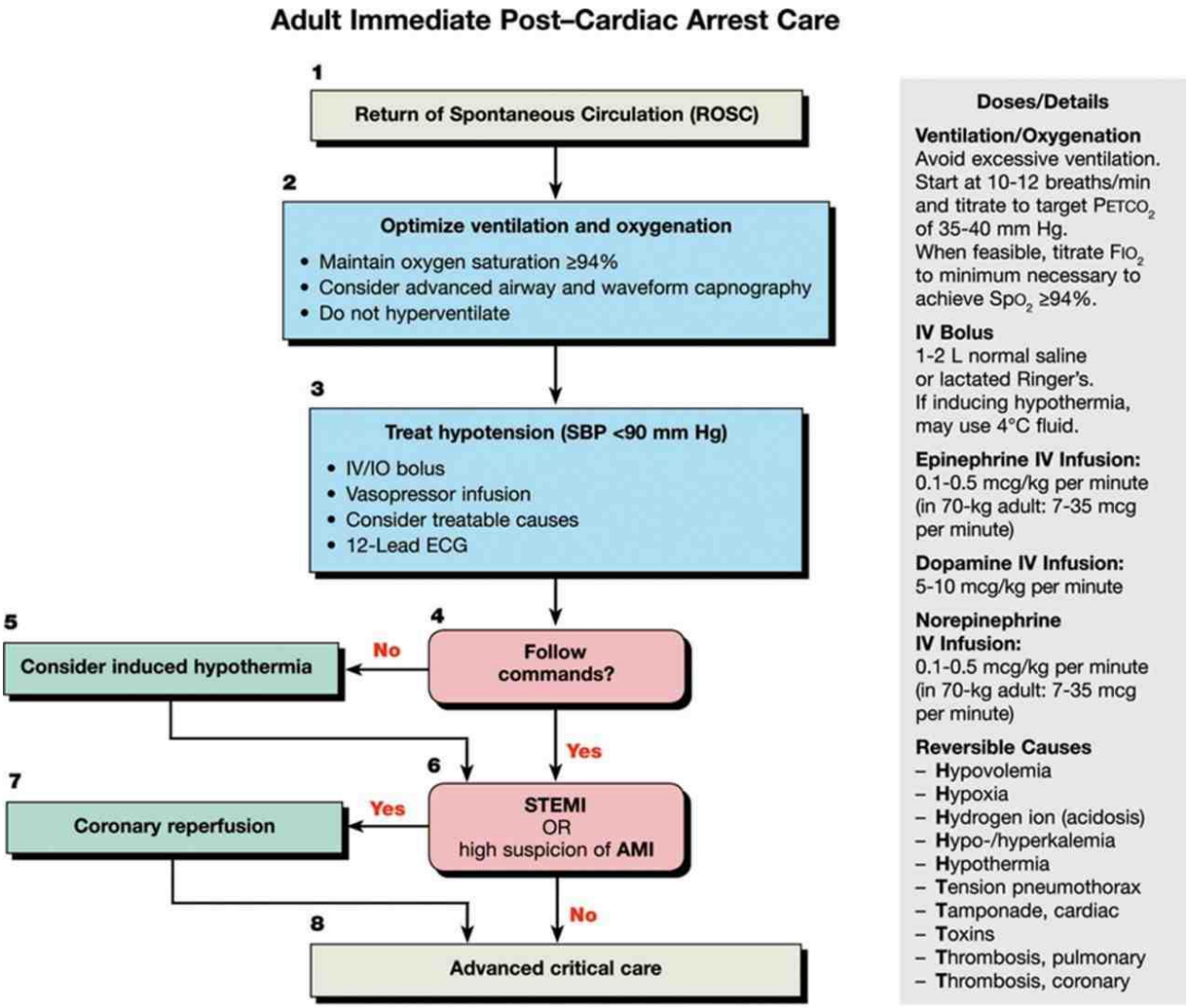

Figure 35: Post-cardiac arrest algorithm

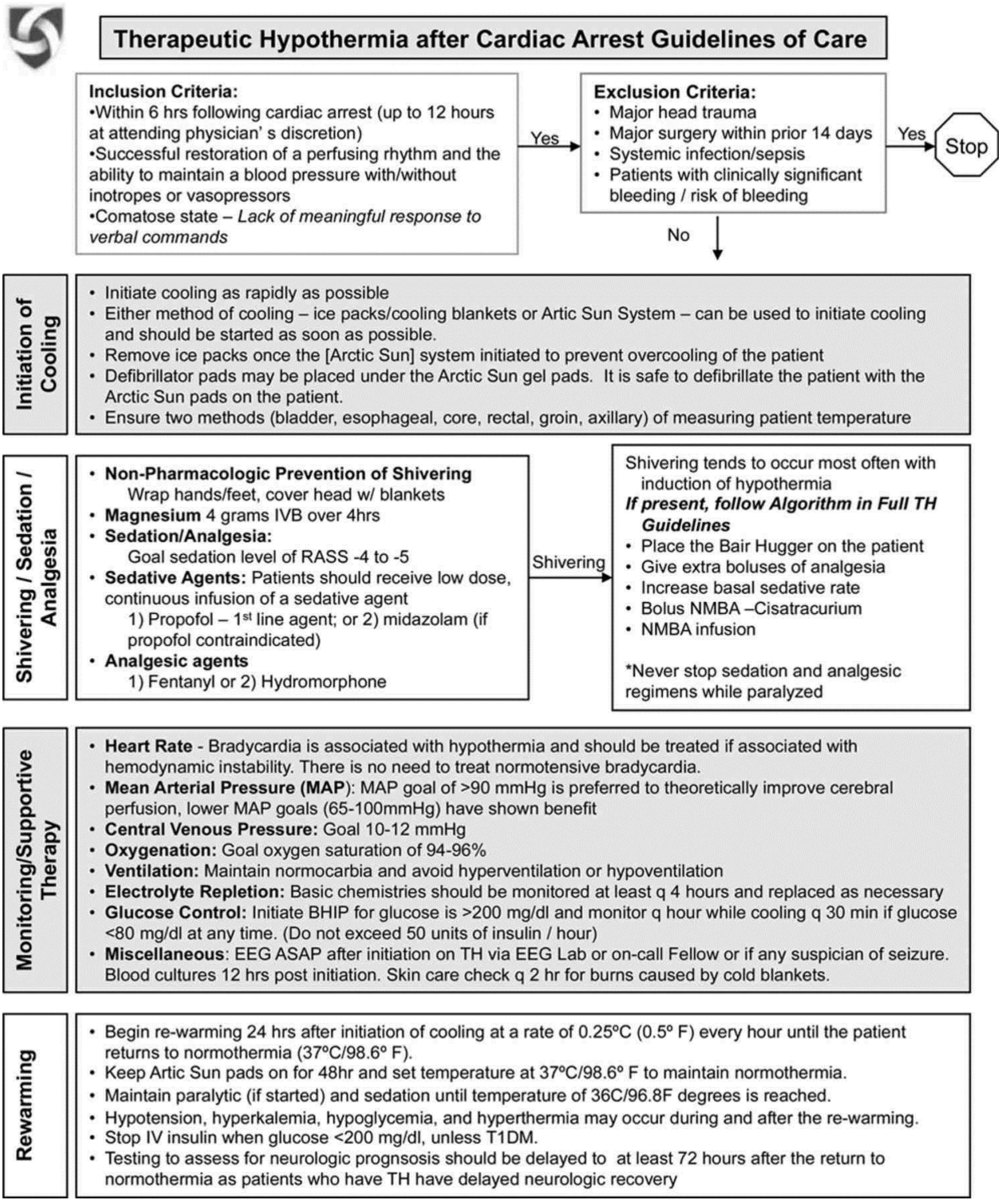

Figure 36: Protocol of induced hypothermia

References

1. Part 9: post-cardiac arrest care: 2010 American Heart Association Guidelines for cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Peberdy MA, Callaway CW, Neumar RW, Geocadin RG, Zimmerman JL, Donnino M, Gabrielli A, Silvers SM, Zaritsky AL, Merchant R, Vanden Hoek TL, Kronick SL; American Heart Association. Circulation. 2010;122:S768-86.

2. Scirica BM. Therapeutic hypothermia after cardiac arrest. Circulation. 2013 ;127:244-50

Postoperative atrial fibrillation (AF)

General principles:

- Beta-blockade should be the first line of therapy for postoperative atrial fibrillation to achieve rapid ventricular rate control and conversion to sinus rhythm
- Amiodarone should be considered as an alternative therapy to beta-blockade for postoperative atrial fibrillation when the patient is hemodynamically unstable or has a known ejection fraction of < 40%. Amiodarone should be dosed as a repeatable 150mg IV bolus followed by 20mg/kg IV for 24 hours. Patients should then be converted to 200mg PO every 8 hours for the first week followed by 200mg PO every twelve hours for three weeks.
- Digoxin, due to its delayed onset of action and ineffectiveness, should not be used for acute rate control in atrial fibrillation, but may have a role for chronic rate control
- During the 48 h after onset of AF, the need for anticoagulation before and after cardioversion may be based on the recommendation of European society of cardiology guidelines of management of AF. (See below)
- AV nodal blocking agents (beta-blockers, calcium-channel blockers, and digoxin) should be avoided in Wolf-Parkinson-White and other pre-excitation syndromes
- Immediate cardioversion with heparinization followed by 4 weeks of anticoagulation may be performed if no atrial thrombus is visualized using transesophageal echocardiography (TEE)
- Electrical cardioversion is indicated in patients with paroxysmal atrial fibrillation and rapid ventricular response who have ECG evidence of acute myocardial infarction or symptomatic hypotension, angina, or heart failure not responsive to pharmacological measures
- Pharmacologic cardioversion by Propafenone: 450-600mg, immediate oral dose (Pill-in-the pocket) approach. Use in conjunction with βblockers or nondihydropyridine calcium blockers.

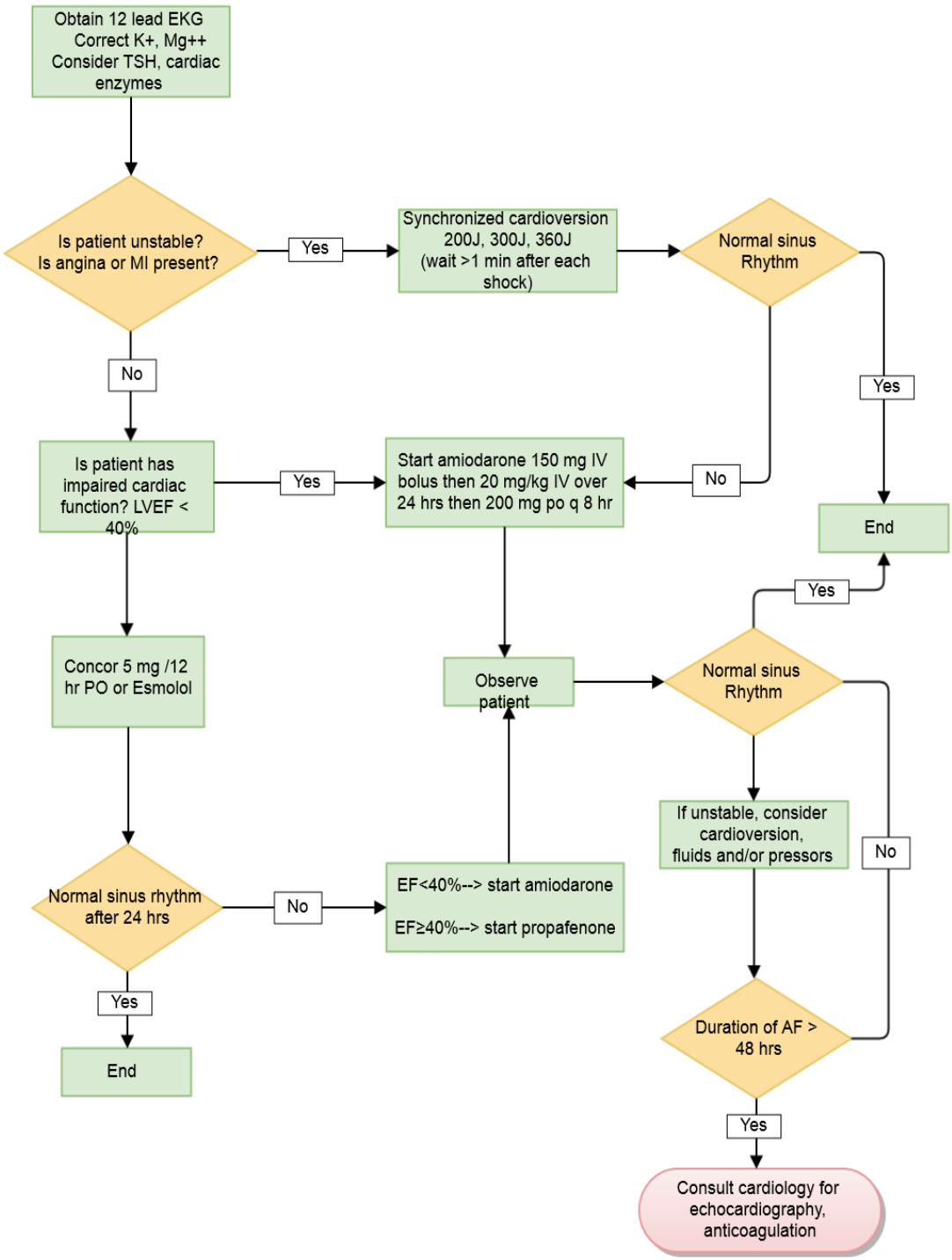

Figure 37: Management of postoperative AF

Choice of Anticoagulant in patient wit AF

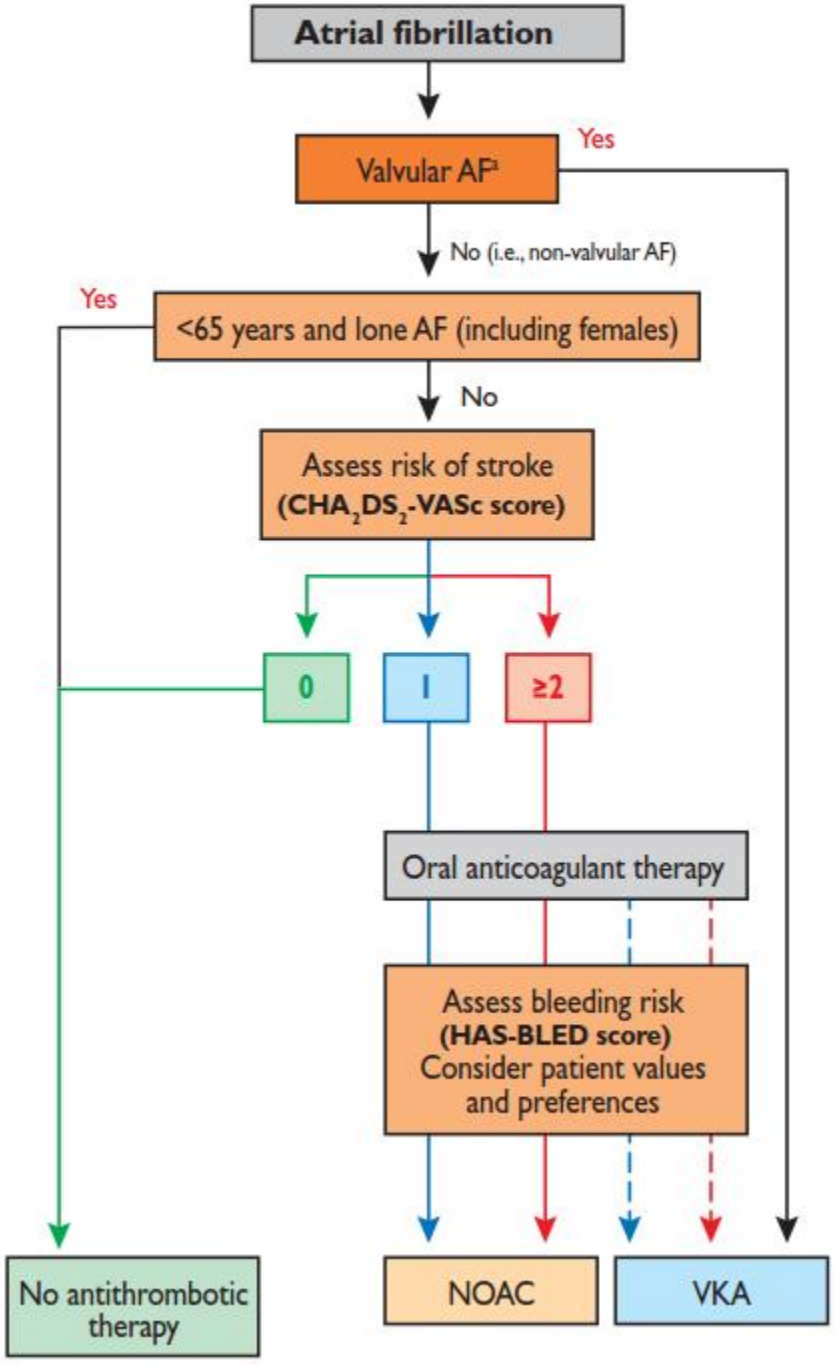

Figure 38: Choice of anticoagulant in patient with AF

Recommendations for prevention of thromboembolism in non-valvular AF

Recommendations	Class[a]	Level[b]
Recommendations for prevention of thromboembolism in non-valvular AF—bleeding		
Assessment of the risk of bleeding is recommended when prescribing antithrombotic therapy (whether with VKA, NOAC, aspirin/clopidogrel, or aspirin).	I	A
The HAS-BLED score should be considered as a calculation to assess bleeding risk, whereby a score ≥3 indicates 'high risk' and some caution and regular review is needed, following the initiation of antithrombotic therapy, whether with OAC or antiplatelet therapy (LoE = A). Correctable risk factors for bleeding [e.g. uncontrolled blood pressure, labile INRs if the patient was on a VKA, concomitant drugs (aspirin, NSAIDs, etc.), alcohol, etc.] should be addressed (LoE = B). Use of the HAS-BLED score should be used to identify modifiable bleeding risks that need to be addressed, but should not be used on its own to exclude patients from OAC therapy (LoE = B).	IIa	A B
The risk of major bleeding with antiplatelet therapy (with aspirin–clopidogrel combination therapy and – especially in the elderly – also with aspirin monotherapy) should be considered as being similar to OAC.	IIa	B
Recommendations for prevention of thromboembolism in non-valvular AF—peri-cardioversion		
For patients with AF of ≥48 h duration, or when the duration of AF is unknown, OAC therapy (e.g. VKA with INR 2-3 or dabigatran) is recommended for ≥3 weeks prior to and for ≥4 weeks after cardioversion, regardless of the method (electrical or oral/i.v. pharmacological).	I	B
In patients with risk factors for stroke or AF recurrence, OAC therapy, whether with dose-adjusted VKA (INR 2-3) or a NOAC, should be continued lifelong irrespective of the apparent maintenance of sinus rhythm following cardioversion.	I	B

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2. Takeshi Omae and Yuichi Kanmura. Management of postoperative atrial fibrillation. J Anesth. 2012; 26: 429–37.

Acute Coronary Syndrome

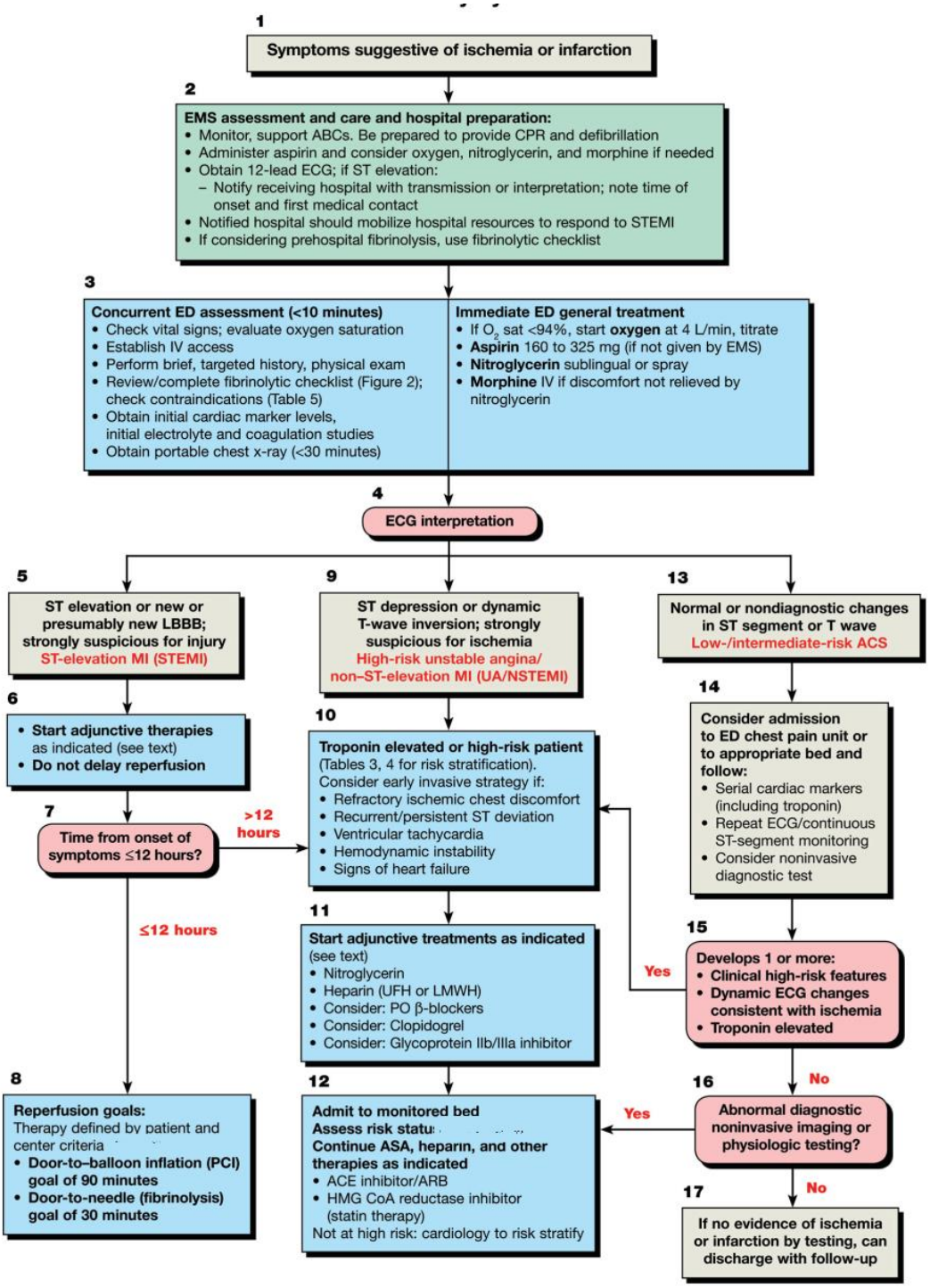

Figure 39: Acute coronary syndrome (1)

Table: Contraindications for fibrinolysis
Absolute contraindications
Haemorrhagic stroke or stroke of unknown origin at any time
Ischaemic stroke in the preceding 6 months
Central nervous system damage or neoplasms
Recent major trauma/surgery/head injury (within the preceding 3 weeks)
Gastro-intestinal bleeding within the last month
Known bleeding disorder
Aortic dissection
Relative contraindications
Transient ischaemic attack in preceding 6 months
Oral anticoagulant therapy
Pregnancy within 1-week post-partum
Non-compressible punctures
Traumatic resuscitation
Refractory hypertension (systole. blood pressure >180 mm Hg
Advanced liver disease
Infective endocarditis
Active peptic ulcer

References

1. O'Connor RE, Brady W, Brooks SC, Diercks D, Egan J, Ghaemmaghami C, Menon V, O'Neil BJ, Travers AH, Yannopoulos D. Part 10: acute coronary syndromes: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010 ;122:S787-817

Pediatric critical care

Pediatric Sepsis & septic shock Resuscitation Management

General Principles:

- Treatment guidelines follow those recommended by the Surviving Sepsis Campaign.

Definitions:

- ***SIRS*** is a response to a stimulus, which results in two or more of the following:

Pediatric age SIRS criteria

Age group	Heart rate		Respiratory rate	Leukocytic count X 10^3/mm	Systolic blood pressure mmHg
0 days to 1 Wk	>180	<100	>60	>34	<59
1 wk to 1 Mo	>180	<100	>50	>19.5 or <5	<75
1 mo to < 2 y	>180	<90	>35	>17.5 or <5	<75
2-5 yrs	>140	Not applicable	>30	>15.5 or <6	<75
6-12 yrs	>130	Not applicable	>20	>13.5 or <4.5	<83
>12 yrs	>110	Not applicable	>20	>11.5 or <4.5	<90

- ***Sepsis:*** is SIRS with a suspected or confirmed bacterial, viral, or fungal cause.
- ***Severe sepsis***: Includes SIRS and at least one of the following signs of hypoperfusion or organ dysfunction that is new and not explained by other known etiology of organ dysfunction:
    - Hypotension < 5 th percentile for age or systolic BP < 2 SD below normal age for age.

- Need for vasoactive drug to maintain BP in normal range (dopamine >5 μg/kg/min or dobutamine, epinephrine at any dose)
- Two of the following:
    - Unexplained metabolic acidosis: base deficit > 5.0 mEg/L
    - Increased arterial lactate > times upper limit of normal
    - Oliguric: urine output <0.5 mL/kg\hr
    - Prolonged capillary refill: > 5 secs
    - Core to peripheral temperature gap > 3°C
- PAO2/FIO2 <300 in absence of cyanotic heart disease or preexisting lung disease
- PaCO2 >65 mmHg or 20 mmHg over baseline PaCO2
- Proven need for >50% FiO2 to maintain saturation ≥ 92%
- Need for nonelective invasive or noninvasive mechanical ventilation
- Glasgow Coma Score ≤11
- Acute change in mental status with a decrease in Glasgow Coma Score ≥3 points from abnormal baseline
- Platelet count < 80,000/mm^3 or a decline of 50% in platelet count from highest value recorded over the past 3 days (for chronic hematology/oncology patients)
- International normalized ratio >2
- Serum creatinine ≥ 2 times upper limit of normal for age or 2-fold increase in baseline creatinine
- Total bilirubin ≥4 mg/dL (not applicable for newborn)
- ALT 2 times upper limit of normal for age

- ***Septic shock:*** is sepsis with fluid refractory hypotension and signs of hypoperfusion.
    - Cold shock: capillary refill >2 sec, decrease peripheral pulse, or mottled cool extremities
    - Warm shock: flash capillary refill, increase peripheral pulse
    - Fluid refractory shock: persistent shock after 60 mL/kg fluid resuscitation
    - Catecholamine resistant shock: Persistent shock after use of direct-acting catecholamines: epinephrine and norepinephrine

Sepsis Protocol:

I. Recognition:

- According to the above criteria, the patient can be categorized as having sepsis, severe sepsis or septic shock.

- Screening: Patients are screened for severe sepsis upon admission and daily thereafter using paper screening sheet (Appendix 1)

II. Septic Shock Resuscitation Bundle

Step 1: Initial resuscitation

- **Zero minutes:**
  - Recognize decreased mental status and perfusion.
  - Maintain & establish vascular access—use intraosseous if IV fails in 90 s.

- **5–15 min :**
  - Push 20 mL/kg normal saline/colloid × 3 up to 60 mL/kg.
  - Assess between each push (Rapid expansion of the liver span, rales and increased work of breathing, enlargement of the cardiac silhouette on chest X-ray, drop in SPO_2.
  - Correct hypoglycemia and hypocalcemia.

Step 2: Manage 15-min fluid-refractory shock

- **15-60 min:**

- Establish central venous access.
- Start dopamine 10 mcg/kg/min.
- Establish arterial access.
- Continue maintenance fluids 4 mL/kg/h and boluses of 0.9% normal saline/colloid as needed.

- **60 minutes have passed—fluid-refractory, dopamine-resistant shock**.
  - When normotensive with a low cardiac output (CO) and high systemic vascular resistance (SVR), initial treatment of fluid-refractory patients consists of the use of an inotropic agent such as dobutamine. Dopamine at a dose of 10–15 m /kg/min should be administered at this time.
  - When hypotensive with a low CO and high SVR (cold shock), EPI (epinephrine) is started at a dose of 0.1 m g/kg and titrated to effect.
  - When BP improves, an inodilator (dobutamine, milrinone, and nitroglycerine) is added to improve tissue perfusion.
  - When hypotensive with a high CO and low SVR (warm shock), then norepinephrine is the vasopressor of choice.

Step 3: Early goal-directed therapy

All four goals to be met for success:

- Normal MAP (>60 mmHg).
- Mixed venous saturation >70%.
- Urine output >1 mL/kg/h.

- CVP >8–12 cm H_2O.

Step 4: Give antibiotics within the first hour and control the source

- Every attempt should be made to get appropriate cultures earlier, but this should not hold up the administration of the drug.
- The choice should be on the basis of the site of infection and local patterns.
- A broad-spectrum antibiotic like a third-generation cephalosporin should be used.
- De-escalate antibiotics once the culture results are available.

Step 5: Mechanical ventilation and sedation

- This step should be considered in any patient who is not rapidly stabilized with fluid resuscitation and peripherally administered inotropes.

Step 6: Give steroids

- If at risk of absolute adrenal insufficiency (e.g., purpura fulminans, congenital adrenal hyperplasia, prior recent steroid exposure as in asthma, or nephrotic syndrome) and remains in shock despite epinephrine or norepinephrine infusion, fluids and inotropes are optimized for an hour (catecholamine resistant shock).
- Hydrocortisone as an intermittent or continuous infusion at 2 mg/kg 6-hourly till hemodynamic stability is achieved.

Step 7: Glucose control

- D5 or D10 for maintenance along with insulin and insulin is titrated to keep blood glucose between 100 and 150 mg/dL. Hyperglycemia should not be treated by reducing fluid concentrations to glucose-free fluids and removing insulin as there is poor glucose utilization and insulin is needed.

Table: Initial Intravenous Pediatric Dosages of Antibiotics for Empiric Treatment of Complicated Intraabdominal Infection		
Antibiotic	**pediatric Dose**	**Frequency of Admonistration**
B lactam/b-lactamase inhibitor combination		
• **Piperacillin tazobactam**	200–300 mg/kg/day of piperacillin component	Every 6–8 h
Carbapenems		
• **Ertapenem** • **Imipenem/cilistatin** • **Meropenem**	15 mg/kg twice daily 60–100mg/kg/day 60mg/kg/day	Every12 h Every 6 h Every 8 h
Cephalosporins		
• **Cefepime** • **Cefotaxime** • **Cefoxitin** • **Ceftazidime** • **Ceftriaxone** • **Cefuroxime**	100 mg/kg/d 150-200 mg/kg/d 160 mg/kg/d 150 mg/kg/d 50-75 mg/kg/d 150mg /kg/d	Every 12 h Every 12 h Every 6–8 h Every 4–6 h Every 8 h Every 12-24 h Every 6–8 h
Tigecycline	100 mg initial dose, then 50 mg every 12 h	
Fluoroquinolones		
• **Ciprofloxacin**	20-30 mg/kg/d	Every 12 h
Metronidazole	6 mg/kg/d	Every 8 h
Clindamycin	20-40 mg/kg/d	Every 6–8 h
Aminoglycosides		
• **Gentamicin or tobramycin** • **Amikacin**	3–7.5 mg/kg/d 15–22.5mg/kg/d	Every 2-4 h Every 8–24 h
Aztreonam	90-120 mg/kg/d	Every 6–8 h
Vancomycin	40 mg/kg	Every 6–8 h

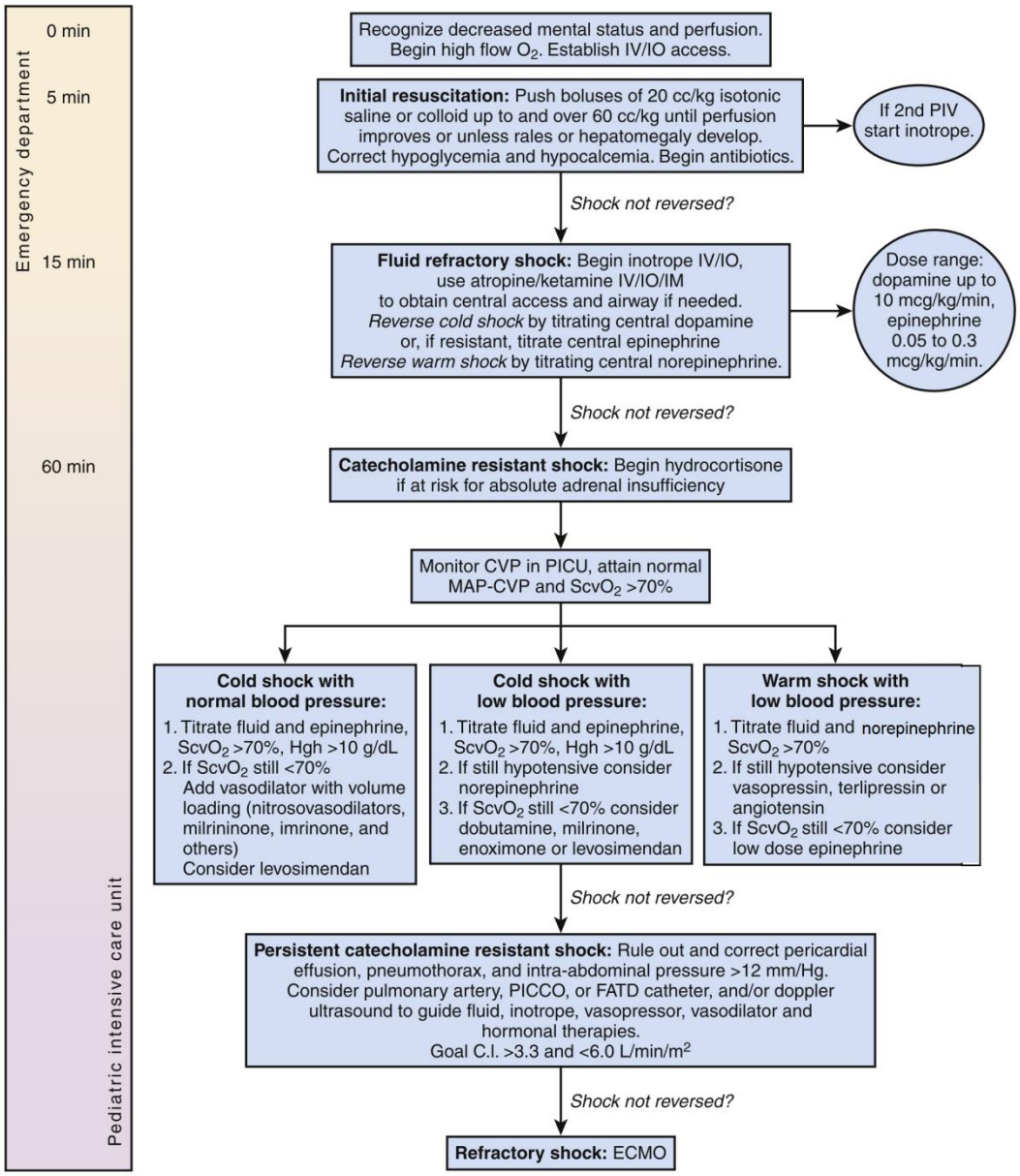

Figure 40: Algorithm for time-sensitive, goal-directed management in children with severe sepsis

References

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2. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med. 2005;6:2-8.

Nutrition

Energy requirement according to the status of patient

Nutrition screening

- Nutritional assessment of critically ill children should be conducted within the first 24 to 48 hours and then at least weekly.
- It should include
  - Weight for age and height/length for age for infants <2 years of age. (*see length for age and weight for age chart*)
  - Body mass index for children >2 years of age (*see BMI chart*)
- Risk of malnutrition include
  - Infant < 2 years
    - Weight for age <3rd percentile
    - Height/length for age <3rd percentile
  - Children ≥ 2 years
    - Underweight children with body mass index (BMI) <5th percentile for age
    - Overweight children with BMI >95th percentile for age
    - Children with a >10% weight loss during their ICU stay
    - Children unable to consistently meet their recommended energy and protein requirements during PICU stay
  - Infant and children on the ventilator for > 7 days
  - Children requiring significant inotropic support or those on muscle relaxants for greater than 7 days

Determining Calorie and Protein Needs in Critically Ill Children

3. Estimate basal energy needs (BEE)

Age 1 wk to 10 mo		**Age 11 to 36 mo**			**Age 3 to 16 yr**		
	Metabolic Rate		Metabolic Rate			Metabolic Rate	
Weight	(kcal/day)	Weight	(kcal/day)		Weight	(kcal/day)	
(kg)	Male or Female		Male	Female	(kg)	Male	Female
3.5	202	9.0	528	509	15	859	799
4.0	228	9.5	547	528	20	953	898
4.5	252	10.0	566	547	25	1046	996
5.0	278	10.5	586	566	30	1139	1092
5.5	305	11.0	605	586	35	1231	1190
6.0	331	11.5	624	605	40	1325	1289
6.5	358	12.0	643	624	45	1418	1387
7.0	384	12.5	662	646	50	1512	1486
7.5	410	13.0	682	665	55	1606	1584
8.0	437	13.5	701	684	60	1699	1680

8.5	463	14.0	720	703	65	1793	1776
9.0	490	14.5	739	722	70	1886	1874
9.5	514	15.0	758	741	75	1980	1973
10.0	540	15.5	778	760			
10.5	566	16.0	797	782			
11.0	593	16.5	816	802			

4. Determine Stress Factor: **Total Calories = BEE X Stress Factor**

Clinical Condition	Stress Factor
Maintenance without Stress	1.0 - 1.2
Fever	12% per degree > 37 C
Routine/elective surgery, minor sepsis	1.1 - 1.3
Cardiac failure	1.25 - 1.5
Major surgery	1.2 - 1.4
Sepsis	1.4 - 1.5
Catch-up Growth	1.5 - 2.0
Trauma or head injury	1.5 - 1.7

5. Estimate patient's protein requirements

Age	g/kg/day
0-6 months	2-3
7-12 months	2-3
13-23 years	2-3
24 months-3 years	1.5-2
4-13 years	1.5-2
14-18 years	1.5

Enteral nutrition in ICU

Timing

- Infants and malnourished children: initiate nutrition, preferably from the enteral route, within 48 hours of admission.
- For older children and those identified to have had good nutritional status prior to admission: initiate nutrition, within 48 - 96 hours of admission.
- Critically ill children who are unable to achieve full enteral feeds in a timely manner and require parenteral nutrition (PN) for the majority of their nutritional support will benefit from the initiation of trophic feedings

- Trophic feedings are typically defined as minimal EN provided at less than 25% of energy needs for the purpose of stimulating the GI tract.

- Contraindication to EN
  - Escalating vasoactive or inotropic support
  - Hemodynamic instability with ongoing volume resuscitation
  - Suspected or confirmed necrotizing enterocolitis or intestinal ischemia
  - Mechanical bowel obstruction
  - Significant gastrointestinal bleeding

Routes

- Nasogastric, orogastric, and transpyloric or nasoduodenal feedings. No preference of one method over another.
- EN may be administered via either continuous or intermittent delivery methods in pediatric who have normal gastric emptying with no gastric distension
- Feeds are switched over to continuous feedings only for those children who do not tolerate the intermittent or bolus schedule

Methods

- Continuous feeding: initiate at 0.5-1 mL/kg/hr or 25/hr maximum
- After 4 hours measure gastric residual volume (GRV) and assess sign of intolerance
- If GRV > 3ml/kg o evidence of intolerance, hold for 1 hour and reassess and if still there is sign of intolerance hold for 4 hours
- If GRV < 3ml/kg, advance by 0.5-1.0 mL/kg/4-6 hrs and assess sign of intolerance
- Signs and symptoms of intolerance
  - Vomiting: 2 or more episodes/24 hours
  - Abdominal discomfort
  - Abdominal distension - 2 consecutive increases of AG in 24 hrs; or AG increase > 2 cm in very low birth weight (VLBW) infants.
  - Diarrhea: 3 or more episodes of loose stool in 24 hours

Risk Factors of aspiration

- Previous history of aspiration
- Altered intestinal motility
- Delayed gastric emptying
- Witnessed regurgitation or aspiration of gastric contents
- Severe gastro-esophageal reflux disease
- Altered mental status with depressed gag and cough reflexes
- Persistent vomiting (2 or more episodes in a 24-hour period)
- Severe bronchospasm
- Noninvasive ventilation (escalating or high settings)

Age/Weight	Initial Infusion Rate	Daily Increases	Goal Rate
2.0 - 15 kg	2 - 15 cc/hr (1 cc/kg/hr)	2 - 15 cc/hr q 4 - 8 hr (1 cc/kg)	15 - 55 cc/hr
16 - 30 kg	8 - 25 cc/hr (0.5 - 1 cc/kg/hr)	8 - 16 cc/hr q 4 - 8 hr (0.5 cc/kg)	45 - 90 cc/hr
30 - 50 kg	15 - 25 cc/hr (0.5 cc/kg/hr)	15 - 25 cc/hr q 4 - 8 hr (0.5 cc/kg)	70 - 130 cc/hr
> 50 kg	25 cc/hr	25 cc/hr q 4 - 8 hr	90 - 150 cc/hr

Intermittent Tube Feeding Progression

Age/Weight	Initial Volumes	Daily Increases	Goal Volume
2.0 - 15 kg	5 - 30 cc q 3 - 4 hr	5 - 30 cc q 6 - 8 hr	50 - 200 q 4 hr
12 - 30 kg	20 - 60 cc q 4 hr	20 - 60 cc q 6 - 8 hr	150 - 350 cc q 4 hr
30 kg	30 - 60 cc q 4 h	30 - 60 cc q 6 - 8 hr	240 - 400 cc q 4 hr

Parenteral nutrition (PN) in ICU

Timing of PN

- If enteral feeds cannot be started, PN should be started by Hospital Day 3 in infants or previously malnourished patients and by Hospital Day 5 in previously well nourished children.

Initiation and advancement

- Parenteral dextrose
    - Begin PN at 10 - 15% dextrose depending on whether the line is peripheral or central and the clinical status and age of the child.
    - Advance by 2.5 - 5% in older infants and children and by 5 - 10% per day in adolescents until an endpoint of D12.5% dextrose for PPN or generally between 20 - 25% dextrose for CPN, as needed to meet nutritional needs (see table below).
    - Glucose infusion rate (GIR)

$$(\frac{\%\ dextrose\ X\ Volume}{Weight})/1.44$$

    - ☐ Example: 10% dextrose with rate 30ml/H (720ml total volume) for 10 kg patient:

$$(\frac{(0.1\ X\ 720}{10})/1.44 = 5$$

- GIR should not exceed 12.5 mg/kg/min in term infant

Age	Initiate	Advance	Maximum
< 1 yr	6-9 mg/kg/min	1-2 mg/kg/min	Goal: 10-12mg/kg/min Max: 12.5mg/kg/min
1-10yr	1-2mg/kg/min	1-2mg/kg/min	Max: 8-10mg/kg/min
>10 yrs (adolescence)	Max: 8-10mg/kg/min	Max: 8-10mg/kg/min	Max: 5-6mg/kg/min

- Parenteral Amino acid
    - Initiation and advancement as shown in table below

Age	Initiate	Advance	Maximum
< 1 yr	1-2 g/kg/day	1 g/kg/day	4 g/kg/day
1-10 yr	1-2 g/kg/day	1 g/kg/day	1.5-3 g/kg/day
>10 yrs (adolescence)	1g/kg/day	1g/kg/day	0.8-2.5g/kg/day

- Parenteral lipid
  - Initiation and advancement as shown in table below
  - Goal is dependent on total kcal goal
  - We should not exceed 60% of total caloric intake via lipid
  - Maximum lipid clearance 0.15 g/kg/hr

Age	Initiate	Advance	Maximum
< 1 yr	1 g/kg/day	1 g/kg/day	3 g/kg/day
1-10 yr	1 g/kg/day	1 g/kg/day	2-3 g/kg/day
>10 yrs (adolescence)	1g/kg/day	1g/kg/day	1-2.5g/kg/day

- Parenteral electrolytes

Electrolyte	Preterm/Neonates	Infant/Children	Adolescence/Children >50 kg
Sodium (mEq)	2-5meq/kg	2-5meq/kg	1-2meq/kg
Potassium (mEq)	2-4meq/kg	2-4meq/kg	1-2meq/kg
Calcium (mEq)	2-4meq/kg	0.5-4meq/kg	10-20meq/day
Phosphate (mEq)	1-2mmol/kg	0.5-2mmol/kg	10-40mmol/day
Magnesium (mEq)	0.3-0.5meq/kg	0.3-0.5meq/kg	10-30meq/day
Chloride (mEq)	As needed to maintain acid-base balance		
Selenium (mcg)	1 - 2 mcg/kg/day		

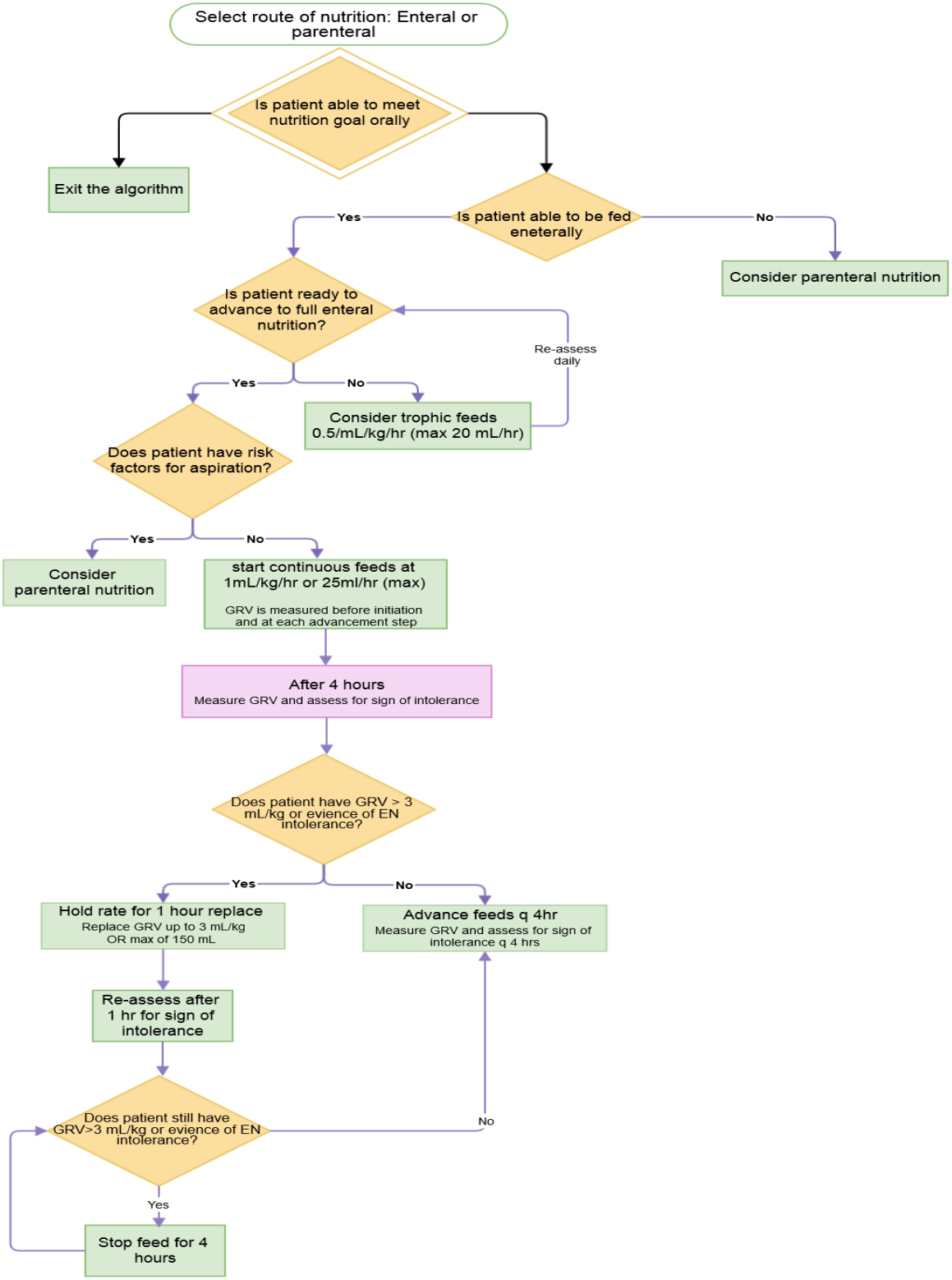

Figure 41: Stepwise algorithm for initiating and advancing enteral nutrition in critically ill pediatric patients.

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Mechanical ventilation

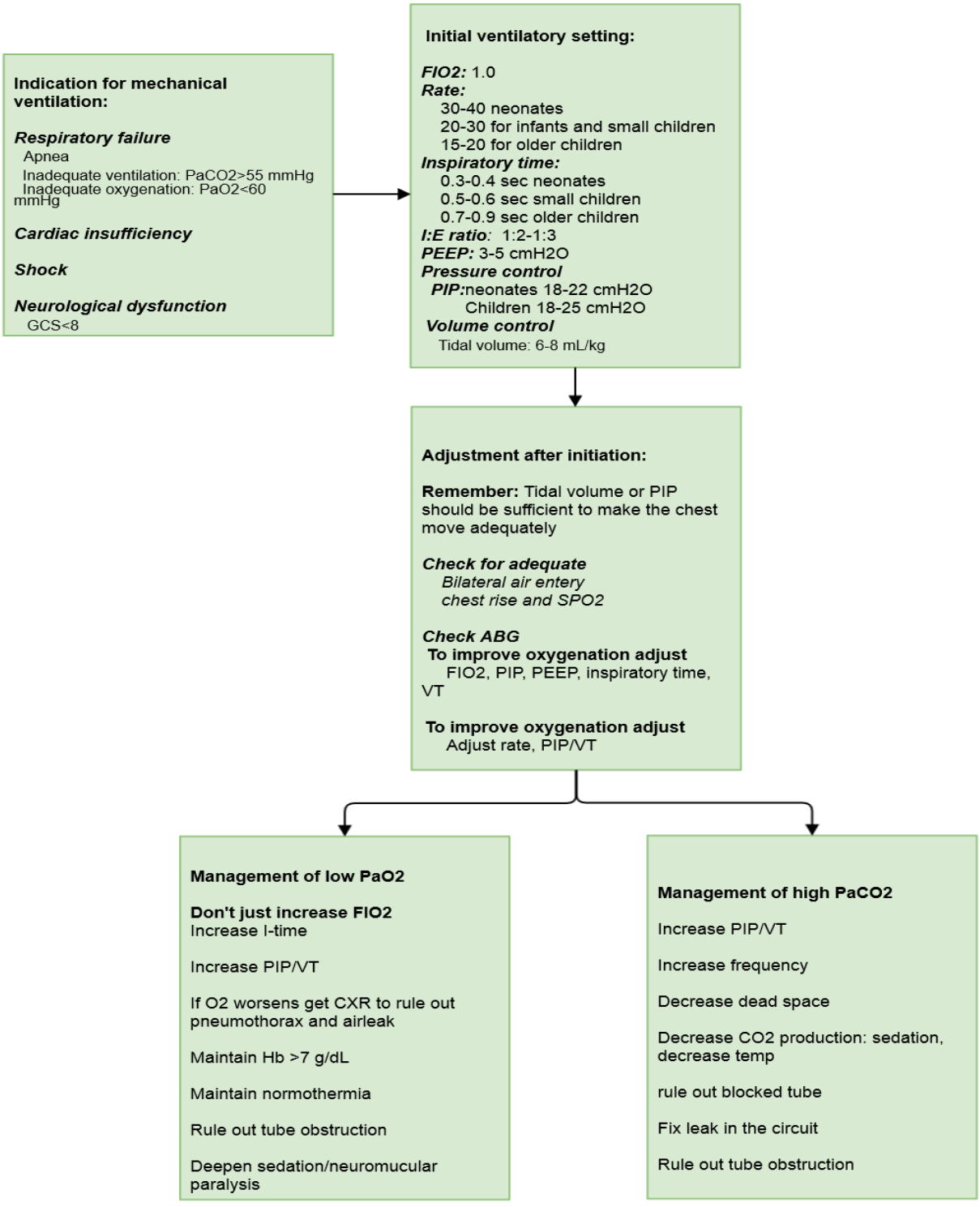

Figure 42: Indication and initial setting of mechanical ventilation

Acute respiratory distress syndrome in pediatrics

General principles

- Although the overall incidence of pediatric ALI is low, the mortality in this population remains high, ranging from 22% to 35%
- The definition of ARDS for infants (older than one month of life), children, and adolescents are essentially identical to those for adults.
- There are intrinsic differences between pediatric patients and adults, which often can affect management strategies which could be summarized as follow:
    - More compliant chest wall
    - Higher sedation requirement
    - Higher baseline airway resistance
    - Low functional residual capacity
- Although the definitive management of ARDS is protective lung strategy, the data for infant and children are lacking

Clinical Management strategy

Initial setting

Tidal volume

- 6-8 mL/kg predicted body weight.

Pressure

- Because many pediatric patients are still ventilated with uncuffed endotracheal tubes, measuring the plateau pressure is not always possible.
- Maintain peak airway pressure < 30 cmH2O
- Minimum PEEP was set at 8-10 cmH2O

Initial inspiratory time

- For infant: 0.4-0.65 s
- For children: 0.5-0.75 s
- For adolescence: 0.7-1:0 s

Initial inspiratory rate:

- For infant: 25-30 breath/min
- For children: 20-25 breaths/min
- For adolescence: 15-20 breaths/min

Subsequent strategies

- Assess oxygenation and ventilation

    - PIP, mean airway pressure, and oxygenation index
- If adequate, continue the previous setting
    - PIP< 30 cmH2O
    - Mean airway pressure < 17 cmH2O
    - Oxygenation index < 15
- If not adequate, consider
    - Recruitment manoeuver
    - Prone position
    - Airway pressure release ventilation
    - Extracorporeal lung oxygenation (ECMO)

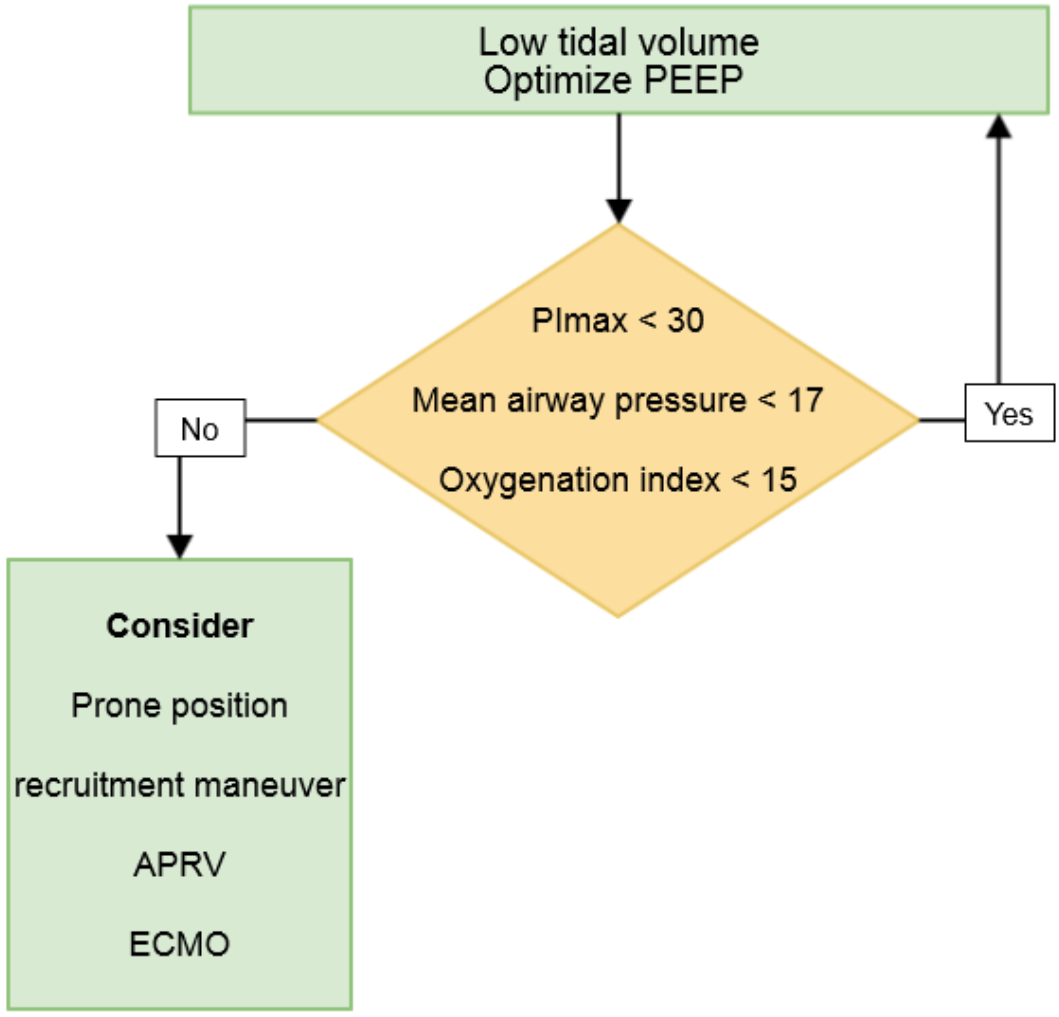

Figure 43: Algorithm of ARDS management in pediatrics

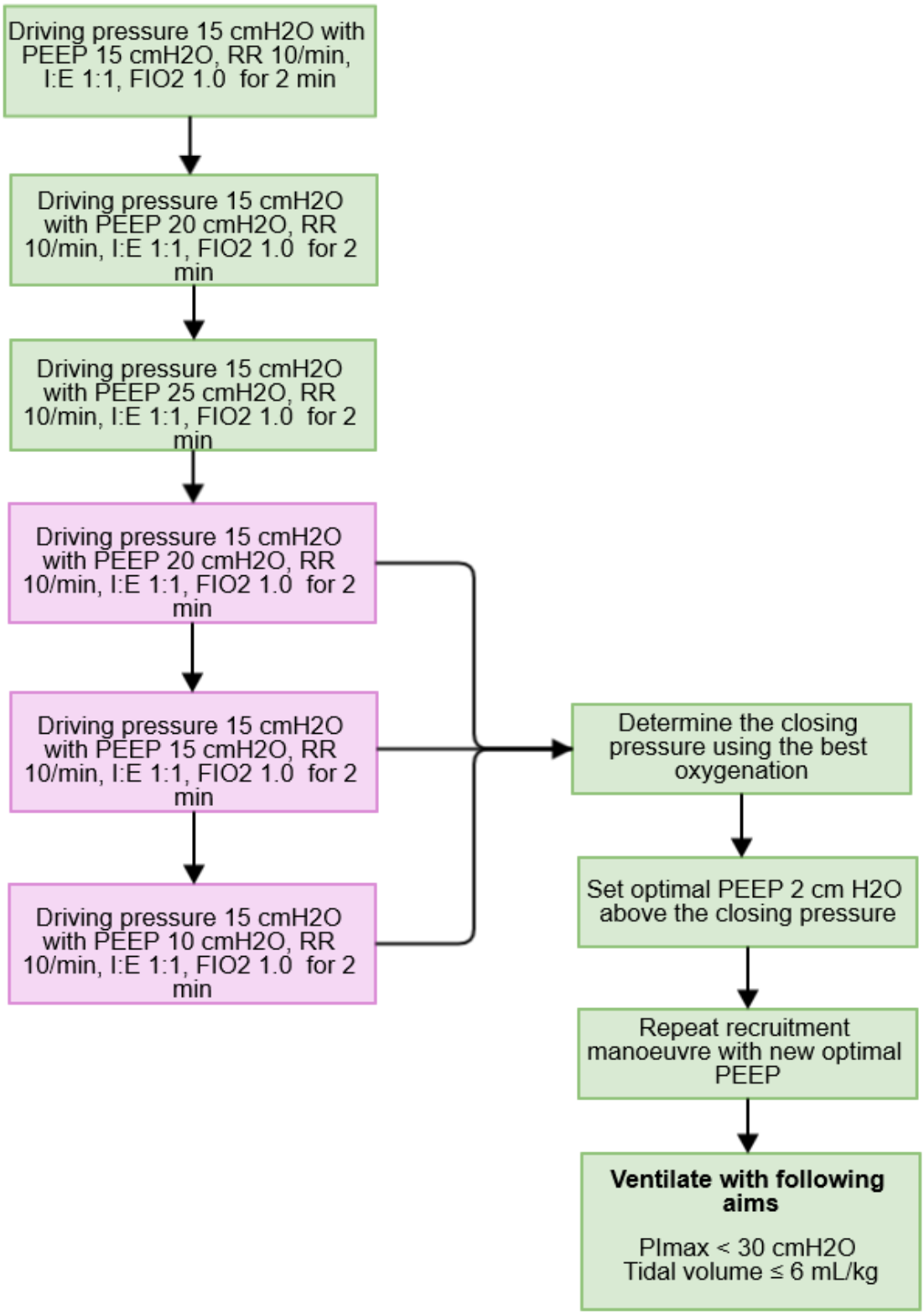

Figure 44: Recruitment manoeuver in critically ill pediatric patients

Weaning of mechanical ventilation in pediatrics

General principles

- Weaning should start when
  - The underlying disease process is improving
  - Gas exchange is adequate
  - No conditions exist that impose an undue burden on the respiratory muscles, such as cardiac insufficiency, severe hyperinflation, severe malnutrition, and multiple organ system failure;
  - The patient is capable of sustaining spontaneous ventilation as ventilator support is decreased without expending an excessive amount of energy.

Assessment of readiness to wean

- Alert mental status
- Good cough and gag reflexes
- Core temperature below 38.5° C
- Spontaneous respiratory effort
- pH 7.32–7.47
- PaO_2 >60 mm Hg or pulse oximetry reading >95%
- $Fio_2 \leq 0.50$
- PEEP ≤7 cm H_2O
- $PaCO_2$ <50 mm Hg
- No further need for vasoactive agents
- No clinical need for increased ventilator support in the past 24 hours
- No planned operative procedures requiring heavy sedation in the next 12 hours

Spontaneous breathing trial

- The SBT can be conducted through
  - Ventilator
    - Use pressure support (PS) ventilation. The minimal PS is adjusted according to size of endotracheal tube
      - PS 10 cmH_2O for ET 3-3.5 mm
      - PS 8 cmH_2O for ET 4-4.5 mm
      - PS 6 cmH_2O for ET ≥ 5 mm
    - The advantage is patient safety as patient is not disconnected from ventilator with monitoring of tidal volume and respiratory rate
  - T-Piece

        - Deliver oxygen enriched gas at high flow rate through a horizontal arm of the T-shaped circuit
- Protocol for SBT
    - Allow 30 to 120 minutes of initial trial of spontaneous breathing
    - SBT is considered failure when patients develop respiratory, cardiovascular, or neurological disability.
- Criteria of failure of SBT
    - Inability to maintain gas exchange
        - Pulse oximeter saturation < 95% with 40% inspired oxygen
        - Needing > 50% inspired oxygen to maintain oxygen saturation > 95%
    - Inability to maintain effective ventilation
        - Measure exhaled tidal volume < 5 mL/kg
        - An increase in PaCO2 > 5 mmHg or an increase of >10 mmHg
        - Respiratory acidosis with PH < 7.3
    - Increased work of breathing
        - Respiratory rate outside of acceptable range for age
            - <6 months: 20–60 breaths/min
            - 6 months to 2 years: 15–45 breaths/min
            - 2–5 years: 15–40 breaths/min
            - >5 years: 10–35 breaths/min
        - Use of accessory respiratory muscle
    - Other signs of respiratory distress
        - Diaphoresis
        - Anxiety
        - Heart rate > 90^{th} percentile for a given age
        - Change in mental status
- Failure of SBT
    - Increase ventilator setting to previously tolerated level or higher if necessary until patient stable again and wait 24 hours before trying again
    - Search for potential reversible etiology

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Obstetrics critical care

General principles

- Initial evaluation and resuscitation of the obstetric patient should focus on airway, breathing and circulation.
- Immediate assessment of gestational age is necessary because of potential aorto-caval compression from the pregnant uterus if >20 weeks gestation.

Respiratory distress in pregnant patient

Causes:

I. Pulmonary causes:
    a. Pulmonary oedema
        i. Pre-eclampsia/Eclampsia
        ii. Tocolytic-induced
        iii. Acute respiratory distress syndrome
    b. Aspiration (Mendelson's syndrome)
    c. Exacerbation of an underlying pulmonary disorder (e.g. asthma)
    d. Pneumomediastinum/pneumothorax
    e. Pneumonia
II. Cardiovascular
    a. Peripartum cardiomyopathy
    b. Pre-existing myopathic or valvular disease
    c. Embolic disorder
        i. Venous thromboembolism
        ii. Amniotic fluid embolism
        iii. Venous air embolism
    d. Anaemia
        i. Dilutional
        ii. Haemorrhage

Hemodynamic instability

Causes

I. Obstetric haemorrhage (particularly post-partum) **MOST IMPORTANT**
II. Sepsis
III. Peripartum cardiomyopathy
IV. Amniotic fluid embolism
V. Pulmonary embolism

VI. Uterine rupture
VII. Epidural/spinal anaesthetic

Resuscitation of the hemodynamically compromized patient

- Establish large bore intravenous access and send blood for
    - Complete blood count
    - Urea, creatinine & electrolytes
    - Liver function tests
    - Acid-base analysis
    - Coagulation screen
    - Group/Type and crossmatch
- Interpretation of laboratory results in hemodynamic compromise requires a knowledge of expected values in a normal pregnancy at a particular gestation
- Basic indicators of tissue perfusion include
    - Level of consciousness (Glasgow coma score)
    - Vital signs
    - Urine output
    - Acid-base status and lactate concentration

Altered mental status/neurological abnormalities

Causes:

- Complication of a pregnancy-specific illness:
    - Eclampsia
    - Acute fatty liver of pregnancy
    - Amniotic fluid embolism
- Pre-existing medical condition that deteriorates during pregnancy:
    - Hypertension (encephalopathy)
    - Intracranial neoplasm
    - Epilepsy
- Obstetric predisposition to particular medical conditions:
    - Cerebral venous sinus thrombosis
    - Hepatitis E infection
    - Subarachnoid haemorrhage

Table 12: Expected values in a normal pregnancy

Parameter	Non-pregnant	Term pregnancy	Impact on resuscitative care
PaO2 (mmHg)	100	103	A rightward shift of the maternal oxyhemoglobin dissociation curve is a compensatory mechanism to improve fetal oxygenation
PaCO2 (mmHg)	40	30	Maintenance of materno-fetal CO2 gradient is important for ongoing fetal CO2 excretion
HCO3 (mmol/L)	24	20	Decrease Buffering capacity, acidosis more likely
White cell count	4-11	6-16	Interpretation of trends in infection more difficult
Creatinine	0.7-1.1	0.6-0.8	Seemingly normal renal indices may indicate renal dysfunction in the parturient
	6.4-8.6 g/dL	4.8-6.4 g/dL	Reduction in albumin:globulin ratio, ↑free fraction of albumin-bound medications ↓ Colloid oncotic pressure
		Transaminase levels - unchanged. Alkaline phosphatase markedly elevated	

Pre-eclampsia

Diagnosis

- Pre-eclampsia is a multisystem disease process. Two cardinal features must exist in order to make the diagnosis:
    - Presence of sustained hypertension
        - Systolic blood pressure >140 mmHg
        - Diastolic blood pressure >90 mmHg
    - Proteinuria
        - >300 mg protein in a 24-hour urine collection
- Severe pre-eclampsia is diagnosed by the presence of
    - Systolic blood pressure >160 mmHg or diastolic blood pressure >110 mmHg on two occasions at least 2 hours apart
    - Proteinuria: >5 g in a 24hr collection
    - Oliguria: <500 mL in 24hr
    - Elevated serum creatinine
    - Pulmonary oedema or cyanosis
    - Persistent headaches
    - Visual disturbances
    - Seizures

Laboratory investigations are necessary to assess the severity of pre-eclampsia

- Complete blood count (to include platelet count)
- Blood urea nitrogen/serum creatinine/serum urate
- Liver function tests (bilirubin/transaminases)
- Coagulation profile
- Blood type (group) and antibody screen
- 24 hour urine collection for protein if time permits
- Chest X-ray if respiratory compromise is present, may identify pulmonary edema
- Non-contrast CT brain or MRI brain if seizures occur, rule out intracranial
- Pathology

Management

- Fluid Balance
    - Increased risk of fluid overload and pulmonary oedema that exists secondary to reduced colloid oncotic pressure
    - No evidence that colloid replacement in pre-eclampsia is superior to crystalloid except perhaps in cases where there is renal or cardiopulmonary compromise
- Blood pressure control

- The goal of antihypertensive treatment is prevention of potential complications such as stroke (intracerebral haemorrhage), cardiac failure and placental abruption
- The threshold for treatment is a diastolic blood pressure (DBP) >110 mmHg and/or systolic blood pressure (SBP) >160 mmHg.
- Slow but steady reduction of SBP to 140-160 mmHg and DBP to 80-110 mmHg with constant fetal monitoring (fetal heart rate) is required
- Drugs commonly used in the acute setting for blood pressure control include
  - labetalol may be administered in bolus form (20-40 mg) I.V. to a maximum of 220 mg with or without a continuous infusion (1-2 mg/min)
  - Hydralazine can be given in 5mg aliquots every 20 minutes to a maximum of 40 mg.
  - Angiotensin-converting enzyme (ACE) inhibitors and angiotensin -2 receptor blockers are both **CONTRAINDICATED** in the acute management of pre-eclampsia secondary to their potential to cause neonatal renal failure and also secondary to their relatively delayed onset of action (1–4 hours)

- Seizure prophylaxis
  - A standard prophylactic and therapeutic MgSO4 regime includes:
  - Loading dose of 4-6 g over 15 min intravenously
  - Maintenance infusion of 1-2 g/hr
  - Target serum concentration of magnesium: 2-3.5 mmol/L (4.8–8.4 mg/dL)
  - Monitoring of magnesium levels
- HELP syndrome
  - Laboratory investigations and results consistent with HELLP include:
    - Peripheral blood smear
      - Presence of burr cells and/or schistocytes indicates microangiopathic haemolytic anaemia
    - Reduced serum haptoglobin levels, elevated serum bilirubin and LDH >600 IU/L are consistent with haemolysis
    - Presence of thrombocytopaenia (Platelet count <100,000/□L)
    - Elevated liver function tests
      - Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) > 70 IU/L
  - A differential diagnosis for HELLP syndrome should include:
    - Acute fatty liver of pregnancy
    - Acute hepatitis
    - Autoimmune thrombocytopenic purpura

        - Thrombotic thrombocytopenic purpura
        - Haemolytic-uremic syndrome
    - Management
        - Delivery of the baby
        - Supportive management

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Peripartum cardiomyopathy

- The diagnosis of peripartum cardiomyopathy requires the presence of the following four criteria:
    - Development of cardiac failure in the last month of pregnancy or within 5 months of delivery (~78% of cases)
    - Absence of any other identifiable cause for the cardiac failure
    - Absence of heart disease prior to last month of pregnancy
    - Echocardiographic evidence of reduced left ventricular function
        - Ejection fraction <45% and/or
        - Fractional shortening <30%
        - End-diastolic dimension >2.7 cm/m2
- Laboratory investigations include:
    - Electrocardiogram
    - Chest X-ray
    - Laboratory Investigations:
        - Full blood count
        - Renal profile
        - Liver function tests
        - Coagulation profile
        - Cardiac enzymes/troponin
        - Arterial blood gas
        - B-type natriuretic peptide
    - Transthoracic echocardiogram
- Management
    - Optimisation of preload
        - Salt and fluid restriction +/- diuretics
        - Continuous venovenous haemofiltration may be required in cases refractory to more conservative measures.
    - Reduction in afterload
        - Vasodilators such as nitroglycerine and/or hydralazine
    - ACE inhibitors are contraindicated antepartum due to potential teratogenic effects but are safe in post-partum and in breast feeding mothers.
    - Hemodynamic support
        - Determined by severity of presentation and response to initial interventions. Inotropic and/or vasopressor support may occasionally be required.
    - Antiarrhythmic therapy should follow normal protocols..

- Anticoagulation should be considered in all patients with peripartum cardiomyopathy because of increased risk of venous thrombo-embolism.
- Immunosuppressive (if myocarditis proven on biopsy) or immunomodulatory therapy may be beneficial in patients when standard treatment has not yielded an adequate response.

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Hemorrhage during pregnancy

- Obstetric blood loss is defined as significant if greater than 1000 mL and major if greater than 2500 mL and/or the transfusion of five or more units of blood and/or requiring treatment for coagulopathy.

Management

- Initial patient evaluation and management should follow the 'ABCDE' approach with early establishment of large bore intravenous access and immediate commencement of fluid resuscitation
- Appropriate monitoring of patients requiring massive transfusion includes:
    - Invasive blood pressure
    - Central venous pressure
    - Urinary output
    - Body temperature
    - Periodic arterial blood gas analysis
    - Periodic coagulation assessment
    - Electrolyte and lactate analysis
- Oxytocin is administered in bolus form, up to 10 IU and also as an infusion usually at a rate of 10 IU/hour.
- Parenteral administration of ergometrine (0.2 mg) results in alpha-adrenergic stimulated contraction of uterine smooth muscle
- Tranexamic acid 1 gm IV to be repeated after 4 hours.
- Recombinant factor VIIa is not recommended by the World Health Organization as a validated therapeutic strategy for PPH

References

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Trauma In Pregnancy

Airway and breathing

- All pregnant trauma patients should receive supplemental oxygen, because the fetus is extremely sensitive to hypoxia.
- In general, pregnancy does not affect the decision to intubate. The use of medications for rapid-sequence intubation in pregnancy is not well studied; however, no absolute contraindications exist.
- If a chest tube is placed, enter the chest 1 or 2 interspaces higher than usual, because the diaphragm is elevated during pregnancy.

Circulation

- Resuscitate the patient with warmed crystalloid administered through large-bore catheters placed for intravenous lines, because as the relative hypervolemia of pregnancy allows for a 30-35% loss of blood volume before hypotension develops.
- Rule out occult sources of bleeding, because maternal blood flow is maintained at the expense of fetal blood flow.
- If blood is needed on an emergency basis, use Rh-negative blood unless the patient's Rh status is known.
- Avoid supine hypotension syndrome, which occurs when the gravid uterus compresses the inferior vena cava by placing rolled towels beneath the spinal board and tilting the patient to the left by 15°.
- If warranted, fetal heart tones may be auscultated as part of the initial fetal assessment and to reassure the mother.

Lab Studies

- Determination of CBC: Pregnancy-induced leukocytosis peaks to levels of 12,000-18,000 per cubic millimeter during the third trimester. During labor, levels as high as 25,000 per cubic millimeter may occur.
- Determination of electrolyte and glucose levels.
- Blood typing and cross matching.
- Rhesus (Rh) blood group determination (administer RhoGAM if the mother is Rh negative).
- Urine pregnancy testing, if the status is unknown in female of reproductive age with trauma
- Urinalysis
- Assessment of coagulation profile
- Toxicology screening
- D-dimer testing helps in determining the course of action for placental abruption.

Imaging Studies:

- Radiologic examinations should not be deferred because of the presence of the fetus.
  - The risk of teratogenesis is greatest from week 1-15 of gestation.
  - Exposure to ionising radiation is expressed in terms of the rad and fetal exposure to <5 rad is considered safe (see below)
- Ultrasonography
    - Assess fetal viability.
    - Assess for multiple gestations.
    - Assess the size, gestational age, and position of the fetus.
    - Ultrasonography can depict free intraperitoneal fluid or hemorrhage in the mother.
- MRI: No report of adverse effects.

Blunt Abdominal Trauma

- Placental Abruption: Over 50% of fetal losses are due to placental abruption (usually occurs within 6 hours of the event). Classic triad of frequent contractions, bleeding and abdominal pain occurs in fewer than half of cases. Ultrasound will identify placental clot only 50% of the time. If mother is hypotensive without a source, consider abruption.
- Uterine Rupture: Not common. Classic presentation is searing pain, abnormalfetal heart rate, and transabdominal palpation of fetal parts
- Fetal-Maternal Hemorrhage: Defined by fetal blood cells in the maternal circulation.
- All pregnant trauma patients with Rh (-) blood type should receive a vial of RhoGam within 72hrs.

Table 13: Fetal exposure during radiological examination of pregnant patient

Procedures	Fetal dose (millirad)
Chest X-ray	<1
Cervical spine plain film	< 1
CT Thorax	30-1300 (mean 600)
CT Abdomen	250
CT Head	< 1000
Helical CT pulmonary angiogram (CTPA	< 50
V/Q scan	< 100
Barium enema	700 -1600

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Cardiac Arrest during pregnancy

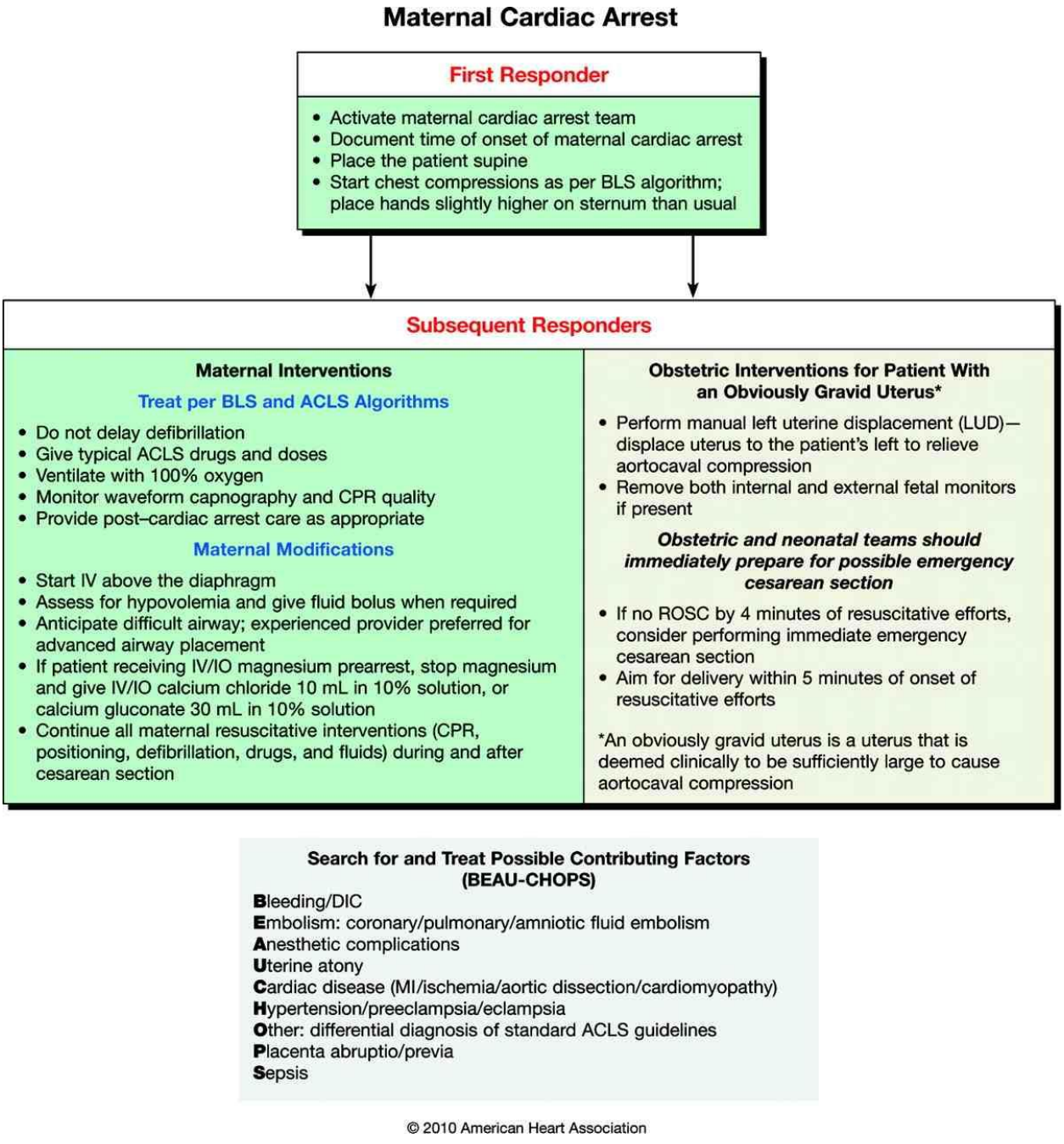

Figure 45: Maternal Cardiac Arrest Algorithm [1]

Figure 46:Left uterine displacement technique (one-handed and two-handed)

Figure 47: Manual leftward uterine displacement-with resuscitation [2]

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Pharmacotherapy

Anticoagulant

Table: Anticoagulants	
Warfarin	• Variable dose ∝ INR • See age-adjusted Warfarin loading protocol below • Daily INR
Heparin (infusion)	• 25000u/50ml = 500u/ml • See below: titrate against APTT: • Cease 4-6 hours prior to surgical procedures
Heparin (sub cut)	• 5000 u sub cut bd <70 kg • 5000 u subcut 8 hrly >70 kg or high risk DVT
Enoxaparin (Clexane®)	• Prophylaxis: 40mg subcut daily 20mg subcut daily if Creat clearance < 30ml/min • Treatment: 1mg/kg subcut bd - lean body mass 1mg/kg subcut once daily if Creat clearance <30ml/min
Fondaparinux (Arixtra)	• Prophylaxis: 2.5 mg subcut daily • Treatment < 50 kg 5 mg sc 50-100 7.5 mg sc > 100 kg 10 mg sc

Heparin Infusion

Table: Heparin infusion protocol

Weight (kg)	45-55	56-65	66-75	76-85	86-95	>95
Bolus (U)	3,500	4,200	4,900	5,600	6,300	7,000
Infusion (U/hr)	900	1,100	1,250	1,400	1,600	1,800

Infusion adjustment

APTT	IV bolus	Stop Infusion	Rate Change	Repeat APTT
< 37	5,000 units		↑ 400u/hr	6 hrs
38-64			↑ 200u/hr	6 hrs
65-110			No change	Daily
111-130			↓ 50u/hr	6 hrs
131-140		30 min	↓ 100u/hr	6 hrs
141-150		60 min	↓ 150u/hr	6 hrs
>150		120 min or APTT < 150	↓ 200u/hr	2 hrs

Note: Infusion: 25,000 units in 50ml syringe = 500U/ml
Check first APTT 6 hrs afcter bolus dose

Warfarin Dosage

General principle

- Warfarin doses should be adjusted to achieve the target INR based on indication as indicated below
- Loading doses of warfarin (i.e. 10 mg) should not be used
- Newly initiated warfarin (or re-initiation) should have daily PT/INR checks, beginning 2-3 days into therapy, until stable
- Patients with significant drug interactions or risk factors should be initiated on a lower dose of warfarin

Thromboembolic risk factors

- Atrial fibrillation
- Left atrium enlargement
- Low left-ventricular ejection fraction
- Age < 70
- Prior thromboembolism
- Hypercoagulable state

Goal and therapeutic INR range

Indication	Target INR	Range	Duration of therapy
Treatment of VTE	2.5	2-3	3 months – lifetime
Atrial Fibrillation	2.5	2-3	Variable
Myocardial infarction			
Antiphospholipid Syndrome	2.5	2-3	Lifetime
Aortic Valve Replacement (AVR) and/or Mitral Valve Replacement (MVR)			
Bioprosthetic (tissue) Valve • **Aortic Valve (AVR)** • **Mitral Valve (MVR)**	2.5	2-3	3 months
Mechanical Prosthetic Valve			
• **Mitral Valve (MVR) – all mitral valves with or without risk factors for thromboembolism1**	3	2.5-3.5	
• **Aortic Valve (AVR)** **o First generation aortic valve (i.e. caged ball or caged disk)**	3	2.5-3.5	
o Modern aortic valve in a patient with normal left atrium and in sinus rhythm	2.5	2-3	Lifetime
o Modern aortic valve with atrial fibrillation or other risk factor(s) for thromboembolism1 **ƒ St. Jude medical bileaflet** **ƒ Carbomedics bileaflet** **ƒ Medtronic Hall tilting disk**	3	2.5-3.5	

Initiation and maintenance

Initiation of warfarin		
Day	INR	Dosage
1		5 mg
2 or 3	< 1.5 1.5-1.9 2-2.5 > 2.5	5 mg 2.5 mg 1-2.5 mg 0 mg
4	< 1.5 1.5-1.9 2-2.5 2.5-3 > 3	5-10 mg 2.5-5 mg 0-2.5 mg 0-2.5 mg 0 mg
5	< 1.5 1.5-1.9 2-3 > 3	10 mg 5-7.5 mg 0-5 mg 0 mg
6	< 1.5 1.5-1.9 2-3 > 3	7.5-12.5 mg 5-10 mg 0-7.5 mg 0 mg

Maintenance of warfarin	
INR	Weekly dose change Dosage
< 1.1	Consider re-initiation
1.1-2.0	Consider increasing weekly dose by 10-20%
2-3	Maintain same dose
3-3.9	Consider decreasing weekly dose by 10-20%
>4	Consider holding a dose and decreasing weekly dose by 20%

Points to remember in initiation therapy

- Check INR at least 4 times during the first week of therapy
- User lower initial dose (2.5-5 mg) if
  - Age > 75,
  - Weight < 60 kg,
  - Interacting medication known to potentiate warfarin,
  - Hepatic dysfunction,
  - Severe heart failure,
  - Renal dysfunction,
  - Hypoproteinemia,
  - Impaired nutritional intake, and
  - Increase in baseline INR (INR > 1.4)
- Use higher initial dose (5-10mg) if: younger patients, interacting medications known to diminish warfarin effects, enteral nutrition, and a diet rich in Vitamin K.

Points to remember in maintenance therapy

- If patient is on outpatient warfarin therapy, use the home dosage as a guide when continuing warfarin therapy in the hospital
- Monitor INR for medication administration changes in interacting drugs, liver function changes, cardiac function changes, and changes in diet
- Once on therapy for > 1 week, dose modifications between 5 to 20% are recommended. Larger change overcorrect abnormally high or low INR
- Recheck an INR within 4-6 days after adjustment for abnormal INR.

Anticoagulant reversal

General Principles

- Management of anticoagulant associated bleeding should follow **HASHTI**
    - ***H***old further doses of anticoagulant
    - Consider ***A***ntidote
    - ***S***upportive treatment: volume resuscitation, inotropes as needed
    - Local or surgical ***H***emostatic measures: topical agents (aminocaproic acid, tranexamic acid)
    - ***T***ransfusion (red cells, platelets, FFP as indicated)
    - ***I***nvestigate for bleeding source
- Reversal of anticoagulant can be classified into two main classes
    - Reversal of Elevated INRs or bleeding patients on anticoagulant/platelet therapy
    - Preoperative management of elevated INRs in patients on warfarin

Reversal of Warfarin

Reversal of Elevated INRs or bleeding patients on Warfarin

Condition	Intervention
INR > goal but < 5 No significant bleeding or risk of bleeding	Lower dose or omit next dose
INR ≥ 5 or < 9 AND No significant bleeding or risk of bleeding	• Preferred: Omit next 1-2 doses • Alternatively, omit 1-2 doses and give Vitamin K (1-2.5 mg po) • Alternatively for patients at high risk of thrombosis (i.e. valves), omit 1-2 doses and use FFP 2 units IV – **DO NOT** use Vitamin K
INR ≥ 9 No significant bleeding AND/OR Low-moderate risk of Bleeding	• Hold warfarin therapy • Give FFP 2 units IV • Give Vitamin K (2.5-5 mg po) • In patients with prosthetic heart valves, give FFP 2 units IV and lower dose of Vitamin K (1-2.5mg po)
Serious bleeding at any elevation of INR AND/OR High risk of bleeding	• **HASHTI** • Give FFP 4 units IV • Vitamin K 10mg by slow IV infusion • May repeat FFP and Vitamin K as needed • In patients with prosthetic heart valves, FFP is preferred over Vitamin K; use only very low doses of Vitamin K (1mg by slow IV infusion)

Preoperative management of elevated INRs in patients on warfarin

- Four doses should be omitted to reduce the INR to ≤ 1.5 in patients taking warfarin with a target INR of 2.5
- Bridging protocol started with therapeutic doses of low molecular weight heparin either 2 or 3 days in advance, and the last dose should be given 24 h before
- INR should be checked on the day before the procedure, enabling vitamin K to be given if the INR is ≥ 1.5
- Postoperative bridging with therapeutic doses should not be restarted within 48–72 h after high bleeding-risk procedures
- Reduced doses, or no bridging at all, should be considered until the bleeding risk has subsided.

INR value	Urgent Surgery or Procedure	Elective Surgery or Procedure (check algorithm below)
INR ≥ 1.5 but ≤ 1.9	Treatment with FFP	• Stop 5 days prior to procedure • Check INR 1-2 days prior ○ If INR >1.5 administer vitamin K 1-2 mg PO
INR > 1.9 but ≤ 5 who require reversal for a procedure No significant bleeding	For rapid (< 12 hours) reversal: FFP + Vitamin K 1-3 mg slow IV	
INR > but < 9 who require surgery No significant bleeding	For rapid (< 12 hours) reversal: FFP + Vitamin K 2-5mg slow IV	

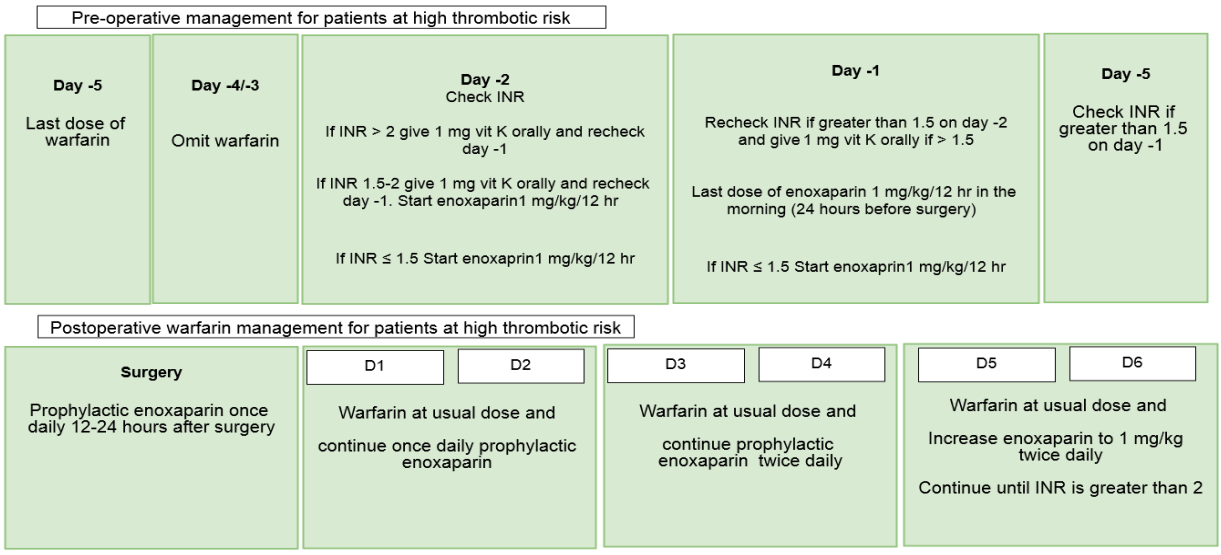


Figure 48: High-risk bridging guidance [3]

Reversal of low molecular weight heparin

Non urgent	Urgent (not bleeding)	Urgent (bleeding)
Hold day of procedure	Wait 12-24 hr if possible	HASHTI
Once daily regimen Half dose day prior	Consider protamine sulfate if delay not possible for high bleeding risk procedure	Protamine sulphate
Twice daily regimen Holding evening dose day prior		Consider recombinant factor VII

Protamine Dose for Reversal of Heparin and LMWH

Agent	Half life	Protamine sulphate dosing for reversal
Heparin	1-2 hr	1 mg per 90-100 units heparin given in previous 2-3 hours • e.g., 25-35 mg if 1000-1250 units/hour heparin Infusion
Enoxaparin	4.5 hours	1 mg per 1 mg Enoxaparin in previous 8 hours
Dalteparin	2.2 hours	1 mg per 100 units Dalteparin in previous 8 hours

New Oral Anticoagulants (NOACs)

General Principles

- The NOACs fall into two classes: the oral direct thrombin inhibitors (e.g. dabigatran) and oral direct factor Xa inhibitors (e.g. rivaroxaban, apixaban, etc.)
- The pharmacokinetics and recommended dosages are explained in table below

	Dabigatran	Rivaroxaban	Apixaban
Drug characteristics			
Mechanism	Oral direct thrombin inhibitor	Oral direct factor Xa inhibitor	Oral direct factor Xa inhibitor
Bioavailability, %	6	60–80	50
Time to peak levels, h	3	3	3
Half-life, h	12–17	5–13	9–14
Excretion	80% renal	2/3 liver, 1/3 renal	25% renal, 75% faecal
Dose	150 mg b.i.d.	20 mg o.d.	5 mg b.i.d.
Dose in renal impairment	110 mg b.i.d.	15 mg o.d. (if CrCl 30-49 mL/min)	2.5 mg b.i.d.
Special considerations	Intestinal absorption is pH-dependent and is reduced in patients taking proton pump inhibitors	Higher levels expected in patients with renal or hepatic failure	
	Increased risk of bleeding in patients taking verapamil/amiodarone/quinidine/ketoconazole	Activity lower in fasted patients so should be taken after food	

Selection of patient groups for warfarin or the new anticoagulants

- For Warfarin
    - Good level of control: patients already taking warfarin with excellent INR control may have little to gain by switching to new oral anticoagulants
    - Renal impairment: warfarin remains the treatment of choice for patients with a calculated creatinine clearance close to or less than 30 mL/min
    - Mechanical heart valve replacement
    - Gastrointestinal diseases: patients with intestinal angiodysplasia, inflammatory bowel disease, or diverticulosis, or those with a history of other forms of gastrointestinal bleeding may experience a deterioration on treatment with new oral anticoagulants
    - Poor compliance: Patients with documented poor adherence to the treatment with warfarin are particularly problematic when switched to new oral anticoagulants.
    - Drug cost
- For the new oral anticoagulants
    - Unexplained poor warfarin control:
    - Poor level of control because of unavoidable drug-drug interactions.
    - New patients on anticoagulant therapy for atrial fibrillation.

Drug interactions with at least 50% change in the exposure to dabigatran or rivaroxaban				
	Dabigatran		Rivaroxaban	
Mechanism	Interacting drug	Δ exposure, %	Interacting drug	Δ exposure, %
P-glycoprotein inhibition	Ketoconazole	150	Ketoconazole	160
	Quinidine	53		
	Amiodarone	60		
	Verapamil	50		
P-glycoprotein induction	Rifampicin	-67	Rifampicin	-50
CYP3A4 inhibition			Ketoconazole	160
			clarithromycin	50
			Ritonavir	50
CYP3A4 induction			Rifampicin	-50

Conversion from warfarin to dabigatran or rivaroxaban

- Starting medication with dabigatran or rivaroxaban when warfarin has been discontinued and the INR has decreased to less than 2.3

Conversion from dabigatran or rivaroxaban to warfarin

Calculated creatinine clearance, mL/mi	Dabigatran: start day with warfarin	Rivaroxaban: start day with warfarin
>50	Day-3	Day-4
31-50	Day-2	Day-3
15-30	Day-1	Day-2
Dabigatran/rivaroxaban is stopped on day 0. The longer overlap with rivaroxaban is justified by its half-life being shorter than that of dabigatran and by the concern about thromboembolic events shortly after transitioning from rivaroxaban to warfarin		

Periprocedural management of dabigatran or rivaroxaban

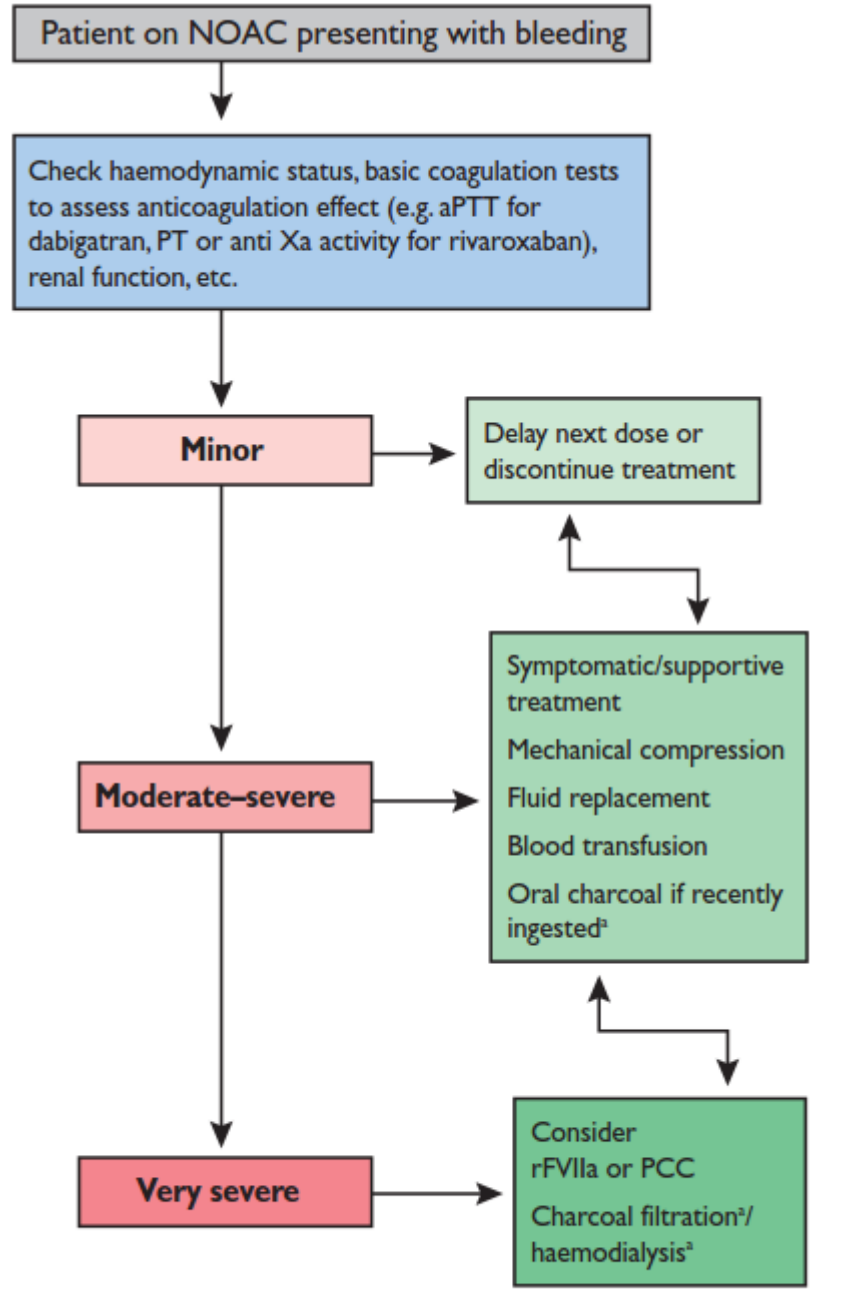
Preoperative management

Timing of interruption of dabigatran or rivaroxaban before surgery or invasive procedures [(2)]			
Calculated creatinine clearance, mL/min	Half-life, hours	Standard risk of bleeding*	High risk of bleeding†
Dabigatran			
>80	13 (11-22)	24 h	2 d
>50-≤80	15 (12-34)	24 h	2 d
>30-≤50	18 (13-23)	2 d	4 d
≤30	27 (22-35)	4 d	6 d
Rivaroxaban			
>30	12 (11-13)	24 h	2 d
≤30	Unknown	2 d	4 d
*Examples are cardiac catheterization, ablation therapy, colonoscopy without removal of large polyps, and lab cholecystectomy			
†Examples are major cardiac surgery, insertion of pacemakers or defibrillators (resulting from the risk for pocket hematoma), neurosurgery, large hernia surgery, and major cancer/urologic/vascular surgery.			

Postoperative management

- The time point for resumption of dabigatran or rivaroxaban depends almost exclusively on the postoperative risk of bleeding.
    - For major abdominal surgery or urologic surgery with incomplete hemostasis, resumption should be delayed until there is no drainage or other evidence of active bleeding.
    - For procedures with good hemostasis shortly after the end of the procedure, same evening a minimum of 4 to 6 hours after surgery.
- The dosage for dabigatran, should be started with a half dose (75 mg) for the first dose
- A similar strategy dose, for rivaroxaban where a 10-mg dose could be used as the first dose.
- Patients with bowel paralysis may require bridging with a parenteral anticoagulants given their inability to take their oral anticoagulant

Reversal of NOACs



aPTT = activated partial thromboplastin time; NOAC = novel oral anticoagulant; PCC = prothrombin complex concentrate; PT = prothrombin time;

Figure 49: Management of bleeding in patient taking NOACs [4]

References:

1. Bonow RO, Carabello BA, Chatterjee K, et.al. 2008 Focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2008;118:e523-661.
2. Schulman S, Crowther MA. How I treat with anticoagulants in 2012: new and old anticoagulants, and when and how to switch. Blood. 2012;119:3016-23
3. Van Veen JJ, Makris M. Management of peri-operative anti-thrombotic therapy. Anaesthesia. 2015 ;70:58-e23
4. Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P; ESC Committee for Practice Guidelines-CPG; Document Reviewers. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation--developed with the special contribution of the European Heart Rhythm Association. Europace. 2012;14:1385-413

Antimicrobial dosing in renal insufficiency

- Dosing recommendations can vary according to indication and patient-specific parameters.
- All dosage adjustments are based on creatinine clearance calculated by Cockcroft-Gault equation

$$Cr\ Cl = \frac{(140 - age)(weight\ in\ kg)}{72(serum\ creatinine)} X\ 0.85\ (if\ femle)$$

Drug	Typical dose (may vary)	CrCl (mL/min)	Dose adjustment for renal insufficiency
Acyclovir IV	5–10 mg/kg Q8H	>50 25–50 10–24 <10 or HD†	5–10 mg/kg Q8H 5–10 mg/kg Q12H 5–10 mg/kg Q24H 2.5–5 mg/kg Q24H
Acyclovir PO (Genital herpes)	200 mg 5x daily	>10 <10	200 mg 5x daily 200 mg Q12H
Acyclovir PO (Herpes Zoster)	800 mg 5x daily	>25 10–25 <10 or HD†	800 mg 5x daily 800 mg Q8H 800 mg Q12H
Amantadine	100 mg Q12H	>50 30–50 15–29 <15 or HD†	100 mg Q12H 200 mg x 1 day, then 100 mg Q24H 200 mg x 1 day, then 100 mg Q48H 200 mg weekly
Amoxicillin	500–1000 mg Q12H	>30 10–30 <10 or HD†	500–1000 mg Q12H 250–875 mg Q12H 250–875 mg Q24H
Amoxicillin (pneumonia)	1 g Q8H	>30 10–30 <10 or HD†	1g Q8H 1g Q12H 1g Q24H
Amoxicillin/ clavulanate	500–1000 mg Q12H	>30 10–30 <10 or HD†	500–1000 mg Q12H 250–500 mg Q12H 250–500 mg Q24H
Amphotericin B	0.7–1 mg/kg Q24H	–	No dosage adjustment
AmBisome®	3–5 mg/kg Q24H	–	No dosage adjustment
Ampicillin	1–2 g Q4–6H	>50 10–50 <10 or HD†	1–2 g Q4–6H 1–2 g Q6–8H 1–2 g Q8H
Ampicillin/ sulbactam	1.5–3 g Q6H	≥30 15–29 ≤14 or HD†	1.5–3 g Q6H 1.5–3 g Q12H 1.5–3 g Q24H
Ampicillin/ sulbactam (for Acinetobacter, *E. faecalis*)	3 g Q4H	≥30 15–29 ≤14 or HD	3 g Q4H 3 g Q6H 3 g Q8H
Azithromycin	250–500 mg Q24H	–	No dosage adjustment
Aztreonam	1–2 g Q8H	≥30 10–29 <10 or HD†	1–2 g Q8H 1–2 g Q12H 1–2 g Q24H

Drug	Typical dose (may vary)	CrCl (mL/min)	Dose adjustment for renal insufficiency
Cefazolin	1–2 g Q8H	≥35 11–34 <10 or intermittent HD HD†	1–2 g Q8H 1 g Q12H 1 g Q24H 2 g Q HD, if HD in 2 days OR 3g Q HD, if HD in 3 days
Cefdinir	300 mg Q12H	≥30 <30 HD†	300 mg Q12H 300 mg Q24H 300 mg QHD
Cefepime	1 g Q8H	>60 30–60 <29 or HD†	1 g Q8H 1 g Q12H 1 g Q24H
Cefepime (Central nervous system infections or *Pseudomonas*)	2 g Q8H	>60 30–60 11–29 <11 or HD†	2 g Q8H 1 g Q8H 1 g Q12H 1 g Q24H
Cefotetan	1–2 g Q12H	≥30 10–29 <10 or HD†	1–2 g Q12H 1–2 g Q24H 500 mg Q24H
Cefpodoxime	100–400 mg Q12H	≥30 <30 HD†	100–400 mg Q12H 100–400 mg Q24H 100–400 mg three times/week
Ceftaroline	600 mg Q12H	>50 30–50 15–29 <15 or HD†	600 mg Q12H 400 mg Q12H 300 mg Q12H 200 mg Q12H
Ceftaroline for MRSA	600 mg Q8H	>50 30–50 15–29 <15 or HD†	600 mg Q8H 400 mg Q8H 300 mg Q8H 400 mg Q12H
Ceftazidime	1–2 g Q8H For *Pseudomonas* 2 g Q8H	>50 30–50 15–29 5–15 HD†	1–2 g Q8H 1–2 g Q12H 1–2 g Q24H 500 mg–1 g Q24H Load with 1 g, then 500 mg Q24H
Ceftriaxone	1–2 g Q24H	–	No dosage adjustment
Ceftriaxone (Central nervous system infections)	2 g Q12H	–	No dosage adjustment
Cephalexin	500 mg PO Q6H	>50 10–50 <10 or HD†	500 mg Q6H 500 mg Q8H 500 mg Q12H
Cidofovir	5 mg/kg Q week for 2 weeks, then every other week	≤55 or Cr>1.5	Not recommended
Ciprofloxacin IV	400 mg Q8–12H	≥30 <30 or HD†	400 mg Q8–12H 400 mg Q24H
Ciprofloxacin PO	250–750 mg Q12H	≥30 <30 or HD†	250–750 mg Q12H 250–500 mg Q24H
Clarithromycin	250–500 mg Q12H	≥30 <30	250–500 mg Q12H 250–500 mg Q24H
Clindamycin	PO: 300 mg Q8H IV: 600 mg Q8H	–	No dosage adjustment
Colistin (Colistimethate)	2.5 mg/kg Q12H	≥50 20–50 ≤20 or HD†	2.5 mg/kg Q12H 2.5 mg/kg Q24H 1.25 mg/kg Q24H

Drug	Typical dose (may vary)	CrCl (mL/min)	Dose adjustment for renal insufficiency
Daptomycin for endocarditis/ bacteremia	6–10 mg/kg Q24H	≥30 <30 HD†	6–10 mg/kg Q24H 6–10 mg/kg Q48H 6–10 mg/kg Q48H
Dicloxacillin	250–500 mg Q6H	–	No dosage adjustment
Doxycycline	100 mg Q12H	–	No dosage adjustment
Ertapenem	1 g Q24H	≥30 <30 or HD†	1 g Q24H 500 mg Q24H
Ethambutol	15–25 mg/kg Q24H	≥10 <10 HD†	Normal dose Q24H Normal dose Q48H Normal dose QHD session
Fluconazole	200–800 mg Q24H	≥50 <50 or HD†	Normal dose (e.g. 100, 400, 800 mg) Q24H Load w/normal dose, then 50% of normal dose Q24H
Flucytosine (5–FC)	12.5–25 mg/kg Q6H	>40 20–40 10–19 <10 or HD†	12.5–25 mg/kg Q6H 12.5–25 mg/kg Q12H 12.5–25 mg/kg Q24H 12.5–25 mg/kg Q24–48H
Ganciclovir (Induction dose)	5 mg/kg Q12H	≥70 50–69 25–49 10–24 <10 or HD†	5 mg/kg Q12H 2.5 mg/kg Q12H 2.5 mg/kg Q24H 1.25 mg/kg Q24H 1.25 mg/kg three times/week, administer after HD
Ganciclovir (Maintenance dose)	5 mg/kg Q24H	≥70 50–69 25–49 10–24 <10 or HD†	5 mg/kg Q24H 2.5 mg/kg Q24H 1.25 mg/kg Q24H 0.625 mg/kg Q24H 0.625 mg/kg three times/week, administer after HD
Gentamicin	–	–	See section on aminoglycoside dosing
Isoniazide	300 mg Q24H	–	No dosage adjustment
Linezolid	600 mg Q12H	–	No dosage adjustment
Meropenem	1 g Q8H	>51 26–50 10–25 <10 or HD†	1 g Q8H 1 g Q12H 500 mg Q12H 500 mg Q24H
Meropenem (Meningitis, CRE infections)	2 g Q8H	>51 26–50 10–25 <10 or HD†	2 g Q8H 1 g Q8H 1 g Q12H 1 g Q24H
Metronidazole	500 mg Q8H	–	No dosage adjustment
Micafungin	100–150 mg Q24H	–	No dosage adjustment
Moxifloxacin	400 mg Q24H	–	No dosage adjustment
Nitrofurantoin (Macrobid®)	100 mg Q12H	≥50 <50	100 mg Q12H Not recommended
Oseltamivir	75 mg Q12–24H	≥30 10–29 <10 or HD†	75 mg Q12–24H 75 mg Q24–48H 30 mg Q every other HD session
Oxacillin	1–2 g Q4–6H	–	No dosage adjustment
Penicillin G	3–4 million units Q4H	≥50 10–49 <10 or HD†	3–4 million units Q4H 1.5 million units Q4H 1.5 million units Q6H

Drug	Typical dose (may vary)	CrCl (mL/min)	Dose adjustment for renal insufficiency
Piperacillin/ tazobactam	3.375–4.5 g Q6H	>40 20–40 <20 HD†	3.375 g Q6H (4.5 g Q6H for *Pseudomonas*) 2.25 g Q6H (3.375 g Q6H for *Pseudomonas*) 2.25 g Q8H (2.25 g Q6H for *Pseudomonas*) 2.25 g Q12H (2.25 g Q8H for *Pseudomonas*)
Posaconazole	400 mg Q12H	–	No dosage adjustment
Pyrazinamide	15–30 mg/kg Q24H	≥10 <10 HD†	15–30 mg/kg Q24H 12–20 mg/kg Q24H 25–30 mg/kg QHD session
Quinupristin/ dalfopristin	7.5 mg/kg Q8H	–	No dosage adjustment
Rifampin (TB)	600 mg Q24H	–	No dosage adjustment
Rifampin	300 mg Q8–12H	–	No dosage adjustment
Rimantadine	100 mg Q12H	>10 ≤10	100 mg Q12H 100 mg Q24H
Telavancin	10 mg/kg Q24H	>50 30–50 10–29 <10 or HD†	10 mg/kg Q24H 7.5 mg/kg Q24H 10 mg/kg Q48H No data
Tigecycline	100 mg once, then 50 mg Q12H	–	No dosage adjustment
TMP/SMX (UTIs or cellulitis)	PO: 1–2 DS tab Q12H IV: 160–320 mg Q12H (Dosing is based on TMP component)	≥30 <30	1–2 DS tab Q12 or 160–320 mg IV Q12H 1–2 DS tab Q24H or 160–320 mg IV Q24H
TMP/SMX (PCP or serious systemic infections)	5 mg/kg Q6–8H	≥30 <30 HD†	5 mg/kg Q6–8H 2.5 mg/kg Q6–8H 2.5 mg/kg Q8H
Valacyclovir (Genital herpes)	500–1000 mg Q12H	≥30 10–29 <10 or HD†	500–1000 mg Q12H 500–1000 mg Q24H 500 mg Q24H
Valacyclovir (Herpes Zoster)	1 g Q8H	≥50 30–49 10–29 <10 or HD†	1 g Q8H 1 g Q12H 1 g Q24H 500 mg Q24H
Valganciclovir (Induction dose)	900 mg Q12H	≥60 40–59 25–39 10–24 <10 or HD†	900 mg Q12H 450 mg Q12H 450 mg Q24H 450 mg Q48H Not recommended
Valganciclovir (Maintenance dose)	900 mg Q24H	≥60 40–59 25–39 10–24 <10 or HD†	900 mg Q24H 450 mg Q24H 450 mg Q48H 450 mg twice weekly Not recommended
Vancomycin	–	–	See section on vancomycin dosing
Voriconazole	See Voriconazole guidelines p. 17	–	No dosage adjustment is necessary for PO. IV should not be administered to patients with CrCl ≤50 mL/min due to accumulation of the vehicle.

Intravenous drug compatibility

IV Compatibilities

The IV compatibility table provides data when 2 or more medications are given into a Y-site of administration. The data in this table largely represent physical incompatibilities (e.g., haze, precipitate, change in color). Therapeutic incompatibilities have not been included, so when using the table, professional judgment should be exercised.

C Physically compatible via Y-site administration.
I Physically incompatible.
N Information on compatibility not available or conflicting

	Dextrose 5%	Sodium Chloride	Acyclovir	Amikacin	Amiodarone	Azithromycin	Aztreonam	Bumetanide	Calcium chloride	Calcium gluconate	Cefazolin	Cefepime	Ceftriaxone	Cimetidine	Ciprofloxacin	Cisatracurium	Dexamethasone	Digoxin	Diltiazem	Diphenhydramine	Dobutamine	Dopamine	Enalapril	Epinephrine	Esmolol	Famotidine	Fentanyl	Fluconazole	Furosemide	Gentamicin	Heparin	Hydrocortisone	Hydromorphone	Imipenem	Insulin, Regular	Ketorolac	Labetalol	Lansoprazole	Levofloxacin	Linezolid	Lorezepam	Magnesium SO_4	Mannitol	Meropenem	Methylprednisolone	Metoclopramide	Metoprolol	Metronidazole	Midazolam	Milrinone	Morphine	Multivitamins	Nitroglycerin	Nitroprusside	Norepinephrine	Ondansetron	Pantoprazole	Phenylephrine	Piperacillin/Tazobactam	Potassium Chloride	Propofol	Ranitidine	Sodium Bicarbonate	Tobramycin	Vancomycin	Vasopressin	Vecuronium
Acyclovir	C	C	—	C	N	N	I	C	N	C	C	I	C	C	I	C	C	N	N	C	I	I	C	I	I	C	C	C	C	C	C	C	C	C	C	N	I	N	I	C	C	C	C	I	C	C	N	C	I	C	I	N	C	I	N	I	N	I	I	C	C	C	C	C	C	N	N
Amikacin	C	C	C	—	C	I	C	C	C	C	C	C	C	I	C	C	C	N	C	C	C	C	C	C	C	C	C	C	C	C	I	C	C	C	N	N	C	C	C	C	C	C	C	N	C	C	N	C	C	C	C	N	C	C	C	C	N	C	C	C	I	C	C	C	C	C	N
Amiodarone	C	N	N	C	—	N	N	C	C	C	N	N	C	N	C	N	N	I	C	N	C	C	N	C	C	C	C	C	N	C	I	N	N	I	C	N	C	N	I	C	C	N	N	N	C	N	N	N	C	C	C	N	C	N	C	N	N	C	I	C	N	N	I	C	C	C	C
Azithromycin	C	C	N	I	N	—	I	N	N	N	N	N	I	N	I	N	N	N	N	C	N	N	N	N	N	I	I	N	I	I	N	N	N	I	N	I	N	N	I	N	N	N	N	N	N	N	N	N	N	N	I	N	N	N	N	C	C	N	I	I	N	N	N	I	N	N	N
Aztreonam	C	C	I	C	N	I	—	C	N	C	C	C	C	C	C	C	C	N	C	N	C	C	C	C	C	C	C	C	C	C	C	C	C	N	C	N	C	I	C	C	I	C	C	N	C	C	N	I	C	N	C	N	C	C	C	C	I	C	C	C	C	C	C	C	N	C	N
Bumetanide	C	C	C	C	C	N	C	—	N	N	C	C	C	N	N	C	C	N	C	C	N	C	C	C	C	C	C	C	C	C	C	C	C	C	C	N	C	N	C	C	C	C	C	N	C	C	N	N	I	C	C	N	C	C	C	C	C	C	C	C	C	N	C	C	C	C	N
Calcium chloride	C	C	N	C	C	N	N	N	—	N	N	N	N	N	N	N	N	N	N	N	C	C	N	C	C	N	N	N	N	N	N	C	N	N	N	N	N	N	N	N	N	I	N	N	N	N	N	N	N	C	C	C	N	C	C	N	I	N	N	I	I	N	I	N	N	N	N
Calcium gluconate	C	C	C	C	C	N	C	N	N	—	C	C	I	N	C	C	I	N	C	C	N	C	C	C	C	C	C	N	C	C	C	N	C	N	C	N	C	I	C	C	C	C	C	C	I	N	N	N	C	C	C	N	C	C	C	C	N	C	C	C	C	N	I	C	C	C	N
Cefazolin	C	C	C	C	N	N	C	C	N	C	—	N	C	N	N	I	C	N	C	I	I	I	C	C	C	N	C	C	C	N	C	C	N	C	C	N	N	I	I	C	C	N	C	N	C	C	N	C	C	C	C	I	C	C	C	C	N	C	N	C	C	C	C	N	N	C	C
Cefepime	C	C	I	C	N	N	C	C	N	C	N	—	N	N	I	N	C	N	I	I	I	I	I	N	N	I	N	C	C	N	C	C	C	C	C	N	N	I	C	C	C	I	I	N	C	I	N	C	I	C	I	N	N	N	N	I	I	N	C	C	N	C	C	N	N	N	N
Ceftriaxone	C	C	C	C	C	I	C	C	N	I	C	N	—	N	N	C	C	N	C	I	I	C	C	C	C	N	C	N	C	N	C	C	C	I	C	N	I	C	C	N	C	I	C	N	C	C	N	C	C	N	C	N	C	C	C	N	C	C	N	C	C	N	C	I	N	C	N
Cimetidine	C	C	C	I	N	N	C	N	N	N	N	N	N	—	N	C	C	C	C	C	C	N	C	C	C	N	C	C	C	N	C	N	C	N	N	N	C	N	C	C	C	N	N	C	C	N	C	C	C	C	C	N	N	C	N	C	N	N	C	C	C	N	N	N	C	N	C
Ciprofloxacin	C	C	I	C	C	I	C	N	N	C	N	I	N	N	—	C	I	C	C	C	C	C	N	N	N	N	N	C	I	C	I	I	C	N	N	N	N	I	N	C	C	I	N	N	I	C	N	C	C	C	N	N	N	N	C	C	I	N	I	C	I	C	I	C	N	C	N
Cisatracurium	C	C	C	C	N	N	C	C	N	C	I	N	C	C	C	—	C	C	C	C	C	C	C	C	C	C	C	C	I	C	I	C	C	C	N	C	N	N	N	C	C	C	C	N	I	C	N	C	C	N	C	N	C	I	C	C	N	C	C	C	I	C	C	C	C	N	N
Dexamethasone	C	C	C	C	N	N	C	C	N	I	C	C	C	C	I	C	—	N	C	I	I	C	C	C	I	C	C	C	C	I	C	C	N	C	C	C	I	C	C	C	C	C	C	C	C	C	N	N	I	C	C	C	C	C	C	C	I	C	C	C	C	N	C	I	N	C	N
Digoxin	C	C	N	N	I	N	N	N	N	N	N	N	N	C	C	C	N	—	C	N	I	N	N	N	C	C	C	I	N	N	C	N	N	N	C	N	N	N	N	C	N	N	N	C	N	N	N	N	C	C	C	N	N	N	N	N	N	N	N	C	I	C	N	N	N	N	N
Diltiazem	C	C	N	C	C	N	C	C	N	C	C	I	C	C	C	C	C	C	—	C	C	C	C	C	C	C	C	C	I	C	N	N	C	C	I	N	C	I	C	C	C	C	C	C	I	C	N	C	C	C	C	N	C	C	C	C	I	C	I	C	N	C	I	C	C	C	C
Diphenhydramine	C	C	C	C	N	C	N	C	N	C	I	I	I	C	C	C	I	N	C	—	C	C	C	C	C	C	C	C	I	C	N	N	C	C	I	N	C	I	C	C	C	C	C	C	I	C	N	N	C	N	C	N	C	I	C	C	I	C	C	C	C	N	I	C	C	C	N
Dobutamine	C	C	I	C	C	N	C	N	C	N	I	I	I	C	C	C	I	I	C	C	—	C	C	C	C	C	C	C	I	C	I	I	C	N	I	N	C	I	C	C	C	N	C	C	C	C	N	N	I	C	C	N	C	N	C	C	I	C	I	C	C	C	I	C	C	C	C
Dopamine	C	C	I	C	C	N	C	C	C	C	I	I	C	N	C	C	C	N	C	C	C	—	C	C	C	C	C	C	I	C	C	C	C	C	N	N	C	I	C	C	C	C	C	C	C	C	N	C	C	C	C	N	C	C	C	C	N	C	C	C	C	C	I	C	C	C	C
Enalapril	C	C	C	C	N	N	C	C	N	C	C	I	C	C	N	C	C	N	C	C	C	C	—	C	C	C	C	C	C	C	C	C	C	C	C	N	C	I	C	C	C	C	C	C	C	C	N	C	C	C	C	N	C	C	C	C	N	C	C	C	C	C	C	C	C	C	N
Epinephrine	C	C	I	C	C	N	C	C	C	C	C	N	C	C	N	C	C	N	C	C	C	C	C	—	C	C	C	C	C	C	C	C	C	C	N	N	C	N	C	C	C	C	C	N	C	C	N	N	C	C	C	C	C	C	C	C	N	C	C	C	C	C	I	C	C	C	C
Esmolol	C	C	I	C	C	N	C	C	C	C	C	N	C	C	N	C	I	C	C	C	C	C	C	C	—	C	C	C	I	C	N	N	C	C	C	N	C	I	C	C	C	C	C	N	N	C	N	C	C	N	C	N	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C
Famotidine	C	C	C	C	C	I	C	C	N	C	N	I	N	N	N	C	C	C	C	C	C	C	C	C	C	—	C	C	I	C	C	C	C	C	N	N	C	I	C	C	C	C	C	N	C	C	N	N	C	N	C	N	C	C	C	C	I	C	I	C	C	N	C	C	C	C	N
Fentanyl	C	C	C	C	C	I	C	C	N	C	C	N	C	C	N	C	C	C	C	C	C	C	C	C	C	C	—	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	N	C	C	N	N	C	C	C	N	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C
Fluconazole	C	N	C	C	C	N	C	C	N	N	C	C	N	C	C	C	C	I	C	C	C	C	C	C	C	C	C	—	I	C	C	C	C	I	C	N	C	C	C	C	C	C	C	C	C	C	N	C	C	N	C	N	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C
Furosemide	N	C	C	C	N	I	C	C	N	C	C	C	C	C	I	I	C	N	I	I	I	I	C	C	I	I	C	I	—	I	C	C	C	C	C	N	N	I	I	C	C	N	C	C	C	I	N	N	I	I	I	N	C	C	N	I	N	N	C	C	C	C	C	C	I	N	I
Gentamicin	C	C	C	C	C	I	C	C	N	C	N	N	N	N	C	C	I	N	C	C	C	C	C	C	C	C	C	C	I	—	I	I	C	C	N	N	C	C	C	C	C	C	C	C	C	C	N	N	C	C	C	C	C	C	C	C	N	C	N	C	I	C	C	C	C	C	C
Heparin	C	C	C	I	I	N	C	C	N	C	C	C	C	C	I	I	C	C	N	N	I	C	C	C	N	C	C	C	C	I	—	N	N	C	C	N	N	C	I	C	C	C	C	C	C	C	N	C	C	C	N	N	C	C	C	C	N	C	C	C	C	C	C	I	I	C	C
Hydrocortisone	C	C	C	C	N	N	C	C	C	N	C	C	C	N	I	C	C	N	N	N	I	C	C	C	N	C	C	C	C	I	N	—	C	C	C	N	I	I	C	C	C	N	C	N	N	C	N	C	I	N	N	N	C	C	C	C	N	C	C	C	C	N	C	N	N	C	C
Hydromorphone	C	C	C	C	N	N	C	C	N	C	N	C	C	C	C	C	N	N	C	C	C	C	C	C	C	C	C	C	C	C	N	C	—	C	C	C	C	I	C	C	C	C	C	C	C	C	N	C	C	C	C	N	C	C	C	C	N	C	C	C	C	C	I	C	C	N	C
Imipenem	N	C	C	C	I	I	N	C	N	N	C	C	I	N	N	C	C	N	C	C	N	C	C	C	C	C	C	I	C	C	C	C	C	—	C	N	C	I	C	C	I	C	I	N	C	C	N	N	I	I	C	N	C	N	C	C	C	C	N	N	C	N	I	C	C	C	N
Insulin, Regular	C	C	C	N	C	N	C	C	N	C	C	C	C	N	N	N	C	C	I	I	I	N	C	N	C	N	C	C	C	N	C	C	C	C	—	N	I	N	I	C	C	C	C	C	C	C	N	N	N	C	N	N	C	C	I	N	N	I	I	C	C	I	C	N	C	N	N

IV Compatibilities

The IV compatibility table provides data when 2 or more medications are given into a Y-site of administration. The data in this table largely represent physical incompatibilities (e.g., haze, precipitate, change in color). Therapeutic incompatibilities have not been included, so when using the table, professional judgment should be exercised.

C Physically compatible via Y-site administration.
I Physically incompatible.
N Information on compatibility not available or conflicting

	Dextrose 5%	Sodium Chloride	Acyclovir	Amikacin	Amiodarone	Azithromycin	Aztreonam	Bumetanide	Calcium chloride	Calcium gluconate	Cefazolin	Cefepime	Ceftriaxone	Cimetidine	Ciprofloxacin	Cisatracurium	Dexamethasone	Digoxin	Diltiazem	Diphenhydramine	Dobutamine	Dopamine	Enalapril	Epinephrine	Esmolol	Famotidine	Fentanyl	Fluconazole	Furosemide	Gentamicin	Heparin	Hydrocortisone	Hydromorphone	Imipenem	Insulin, Regular	Ketorolac	Labetalol	Lansoprazole	Levofloxacin	Linezolid	Lorezepam	Magnesium SO_4	Mannitol	Meropenem	Methylprednisolone	Metoclopramide	Metoprolol	Metronidazole	Midazolam	Milrinone	Morphine	Multivitamins	Nitroglycerin	Nitroprusside	Norepinephrine	Ondansetron	Pantoprazole	Phenylephrine	Piperacillin/Tazobactam	Potassium Chloride	Propofol	Ranitidine	Sodium Bicarbonate	Tobramycin	Vancomycin	Vasopressin	Vecuronium
Ketorolac	C	C	N	N	N	I	N	N	N	N	N	N	N	N	N	C	C	N	N	N	N	N	N	N	N	N	C	N	N	N	N	N	C	N	N	—	N	N	N	N	C	N	I	N	N	N	N	N	N	N	C	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Labetalol	C	C	I	C	C	N	C	C	N	C	N	N	I	C	N	N	I	N	C	C	C	C	C	C	C	C	C	C	N	C	N	I	C	C	I	N	—	I	C	C	C	C	C	N	C	C	N	C	C	C	N	N	C	C	C	C	I	C	I	C	C	C	N	C	C	C	C
Lansoprazole	C	C	N	C	N	N	I	N	N	I	I	I	C	N	I	N	C	N	I	I	I	I	I	N	I	I	C	C	I	C	C	I	I	I	N	N	I	—	I	N	I	I	C	N	I	I	N	I	I	N	I	N	I	N	N	I	N	I	C	I	N	N	I	I	I	N	N
Levofloxacin	C	C	I	C	I	I	C	C	N	C	I	C	C	C	N	N	C	N	C	C	C	C	C	C	C	C	C	C	I	C	I	C	C	C	I	N	C	I	—	C	N	C	N	N	C	C	N	C	C	N	C	N	I	I	N	C	I	C	I	C	I	N	C	C	C	N	N
Linezolid	C	C	C	C	C	N	C	C	N	C	C	C	N	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	N	C	N	C	—	C	C	C	C	C	C	N	C	C	N	C	N	C	C	C	C	I	C	C	C	N	C	C	C	C	C	C
Lorazepam	C	C	C	C	C	N	I	C	N	C	C	C	C	C	C	C	C	N	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	C	C	I	N	C	—	C	C	C	C	C	N	C	C	C	C	N	C	C	C	I	I	C	C	C	C	C	C	C	C	C	C
Magnesium SO_4	C	C	C	C	N	N	C	C	I	C	N	I	I	N	I	C	C	N	C	C	N	C	C	C	C	C	C	C	N	C	C	N	C	C	C	N	C	I	C	C	C	—	C	C	I	C	N	C	C	C	C	N	C	C	C	C	N	C	C	C	C	N	N	C	C	C	N
Mannitol	C	C	C	C	N	N	C	C	N	C	C	I	C	N	N	C	C	N	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	I	C	C	N	C	C	C	—	I	C	C	N	N	C	N	C	I	C	C	C	C	N	C	C	C	C	N	C	C	C	C	N
Meropenem	I	C	I	N	N	N	N	N	N	C	N	N	N	C	N	N	C	C	C	C	C	C	C	N	N	N	N	C	C	C	C	N	C	N	C	N	N	N	N	C	C	C	I	—	N	C	N	N	N	C	C	N	N	N	C	I	N	N	N	N	N	C	I	N	C	C	N
Methylprednisolone	C	C	C	C	C	N	C	C	N	I	C	C	C	C	I	I	C	N	I	I	C	C	C	C	N	C	C	C	C	C	C	N	C	C	C	N	C	I	C	C	C	I	C	N	—	C	N	C	C	C	C	N	C	C	C	I	I	C	C	N	I	C	C	C	C	C	N
Metoclopramide	C	C	C	C	N	N	C	C	N	N	C	I	C	N	C	C	C	N	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	C	N	C	I	C	C	C	C	C	C	C	—	N	N	C	N	C	C	C	C	C	C	N	C	C	C	I	C	C	C	C	C	N
Metoprolol	C	C	N	N	N	N	N	N	N	N	N	N	N	C	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	—	N	N	N	C	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Metronidazole	C	C	C	C	N	N	I	N	N	N	C	C	C	C	C	C	N	N	C	N	N	C	C	N	C	N	N	C	N	N	C	C	C	N	N	N	C	I	C	C	C	C	N	N	C	N	N	—	C	C	C	N	N	N	N	N	I	N	C	N	N	N	N	N	N	C	N
Midazolam	C	C	I	C	C	N	C	I	N	C	C	I	C	C	C	C	I	C	C	C	I	C	C	C	C	C	C	C	I	C	C	I	C	I	N	N	C	I	C	C	C	C	C	N	C	C	N	C	—	C	C	N	C	C	C	C	I	C	I	C	N	C	I	C	C	C	C
Milrinone	C	C	C	C	C	N	N	C	C	C	C	C	N	C	C	N	C	C	C	N	C	C	C	C	N	N	C	N	I	C	C	N	C	I	C	N	C	N	N	N	C	C	N	C	C	N	N	C	C	—	C	N	C	C	C	N	N	N	C	C	C	C	C	C	C	C	C
Morphine	C	C	I	C	C	I	C	C	C	C	C	I	C	C	N	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	N	N	C	C	N	C	N	I	C	C	C	C	C	C	C	C	C	C	C	C	—	N	C	C	C	C	N	C	C	C	N	C	N	C	C	C	C
Multivitamins	C	C	N	N	N	N	N	N	C	N	I	N	N	N	N	N	C	N	N	N	N	N	N	C	N	N	N	N	N	C	N	N	N	N	N	N	N	N	N	N	N	N	I	N	N	C	N	N	N	N	N	—	N	N	C	N	N	N	N	N	N	N	C	N	N	N	N
Nitroglycerin	C	C	C	C	C	N	C	C	N	C	C	N	C	N	N	C	C	N	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	N	C	I	I	C	C	C	C	N	C	C	N	N	C	C	C	N	—	C	C	C	N	C	C	C	C	C	C	C	C	C	C
Nitroprusside	C	C	I	C	N	N	C	C	C	C	C	N	C	C	N	I	C	N	C	I	N	C	C	C	C	C	C	C	C	C	C	C	C	N	C	N	C	N	I	C	C	C	C	N	C	C	N	N	C	C	C	N	C	—	C	C	N	C	C	C	C	C	C	C	C	C	C
Norepinephrine	C	N	N	C	C	N	C	C	C	C	C	N	C	N	C	C	C	N	C	C	C	C	C	C	C	C	C	C	N	C	C	C	C	C	I	N	C	N	N	C	C	C	C	C	C	C	N	N	C	C	C	C	C	C	—	C	N	C	C	C	C	C	I	C	C	C	C
Ondansetron	C	C	I	C	N	C	C	C	N	C	C	I	N	C	C	C	C	N	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	N	N	C	I	C	C	I	C	C	I	I	C	N	N	C	N	C	N	C	C	C	—	I	C	C	C	C	C	I	C	C	C	N
Pantoprazole	C	C	N	N	N	C	I	C	I	N	N	I	C	N	I	N	I	N	I	I	I	N	N	N	I	I	I	I	N	N	N	N	N	C	N	N	I	N	I	I	I	N	N	N	I	N	N	I	I	N	N	N	N	N	N	I	—	C	N	C	N	N	N	N	N	C	N
Phenylephrine	C	C	I	C	C	N	C	C	N	C	C	N	C	N	N	C	C	N	C	C	C	C	C	C	C	C	C	C	N	C	C	C	C	C	I	N	C	I	C	C	C	C	C	N	C	C	N	N	C	N	C	N	C	C	C	C	C	—	C	C	N	N	C	C	C	C	N
Piperacillin/Tazobactam	C	C	I	C	I	I	C	C	N	C	N	C	N	C	I	C	C	N	I	C	I	C	C	C	C	I	C	C	C	N	C	C	C	N	I	N	I	C	I	C	C	C	C	N	C	C	N	C	I	C	C	N	C	C	C	C	N	C	—	C	N	C	C	I	I	C	N
Potassium Chloride	C	C	C	C	C	I	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	N	C	N	C	I	C	C	C	C	C	N	N	C	N	N	C	C	C	N	C	C	C	C	C	C	C	—	C	C	C	C	C	C	N
Propofol	C	N	C	I	N	N	C	C	I	C	C	N	C	C	I	I	C	I	N	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	N	C	N	I	N	C	C	C	N	I	I	N	N	N	C	N	N	C	C	C	C	N	N	N	C	—	C	C	I	N	N	C
Rantidine	C	C	C	C	N	N	C	N	N	N	C	C	N	N	C	C	N	C	C	N	C	C	C	C	C	N	C	C	C	C	C	N	C	N	I	N	C	N	N	C	C	N	N	C	C	C	N	N	C	C	C	N	C	C	C	C	N	N	C	C	C	—	N	N	C	N	C
Sodium Bicarbonate	C	C	C	C	I	N	C	C	I	I	C	C	C	N	I	C	C	N	I	I	I	I	C	I	C	C	C	C	C	C	C	C	I	I	C	N	N	I	C	C	C	N	C	I	C	C	N	N	I	C	N	N	C	C	I	I	N	C	C	C	C	N	—	C	N	C	N
Tobramycin	C	C	C	C	C	I	C	C	N	C	N	N	I	N	C	C	I	N	C	C	C	C	C	C	C	C	C	C	C	C	I	N	C	C	N	N	C	I	C	C	C	C	C	N	C	C	N	N	C	C	C	N	C	C	C	C	N	C	I	C	I	N	C	—	C	C	N
Vancomycin	C	C	C	C	C	N	N	C	N	C	N	N	N	C	N	C	N	N	C	C	C	C	C	C	C	C	C	C	I	C	I	N	C	C	C	N	C	I	C	C	C	C	C	C	C	C	N	N	C	C	C	N	C	C	C	C	N	C	I	C	N	C	N	C	—	C	C
Vasopressin	C	C	N	C	C	N	C	C	N	C	C	N	C	N	C	N	C	N	C	C	C	C	C	C	C	C	C	C	N	C	C	C	N	C	N	N	C	N	N	C	C	C	C	C	C	C	N	C	C	C	C	N	C	C	C	C	C	C	C	C	N	N	C	C	C	—	N
Vecuronium	C	C	N	N	C	N	N	N	N	N	C	N	N	C	N	N	N	N	C	N	C	C	N	C	C	N	C	C	I	C	C	C	C	N	N	N	C	N	N	C	C	N	N	N	N	N	N	N	C	C	C	N	C	C	C	N	N	N	N	N	C	C	N	N	C	N	—

Pediatric drug infusion

Drug (inf = infusion)	*Dose range*	*1ml/hr =*	*Add to 50ml*	*Notes*
Adrenaline (inf)	0.1-2.0 mcg/kg/min	0.1 mcg/kg/min	0.3 mg x wt	Intravenous, intraosseous. Always via CENTRAL line. In 5%dex or 0.9% N/S
Aminophylline (inf)	1 mg/kg/hr	1 mg/hr	x wt	Load 5mg/kg unless previous aminophylline. FIXED concentration mg/ml. Dose reduced infusion with age. Therapeutic range 10-20mg/l. Toxic tachycardia, jittery, seizures. Dilute in 5% dex
Amiodarone (inf)	5-15 mcg/kg/min	5 mcg/kg/min	15 mg x wt	Load 25mcg/kg/min for 4 hrs if no previous amiodarone . Baseline thyroid and liver functions. Only dilute in 5% dex. Not <600mcg/ml. Max 1.2g/24hrs. Baseline eye exam /TFT
Dobutamine (inf)	5-20 mcg/kg/min	10 mcg/kg/min	30 mg x wt	Vasodilatation and tachycardia. Central administration preferred if >5mg/ml.
Dopamine (inf)	5- 20 mcg/kg/min	10 mcg/kg/min	30 mg x wt	Central administration recommended. For peripheral administration 3x wt in mg (maximum 1.6mg/ml). Dilute in 5% dex or 0.9% N/S.
Esmolol (inf)	25-200 mcg/kg/min		x wt	Loading dose 500mcg/kg over 1 minute. Dilute to 10mg/ml through large bore vein. Dilute in 5% dex or 0.9% N/S. Recommended max concentration 20mg/ml (central administartion). Extravasation risk.
Fentanyl (inf)	1-5 mcg/kg/hr	1 mcg/kg/hr	50 mcg x wt	Usual dose 1 - 3 mcg/kg/hr. Cumulative effect. Risk of rigid chest in neonates. Discuss with consultant. Dilute in 5% dex or 0.9% N/S.
Furosemide (inf)	0.1- 1 mg/kg/hr	0.2 mg/kg/hr	10 mg x wt	Dilute in 0.9% N/S only. For concentrated infusions 50 x wt in mg = 1mg/kg/hr= 1 ml/hr. Incompatible with most common infusions
GTN (Glycerine trinitrate) (inf)	1- 5 mcg/kg/min	1 mcg/kg/min	3 mg x wt	Tachyphylaxis may occur after 24 hrs. Recommended maximum concentration 400mcg/ml. In fluid restricted patients 1mg/ml centrally
Heparin (inf)	10-30 units/kg/hr	20 units/kg/hr	1000 units x wt	Use APTT to direct therapy.Load 75units/kg. Start infusion at 20 units/kg/hr
Insulin (inf)	0.01- 0.2 u/kg/hr	0.05 u/kg/hr	2.5 units x wt	Dilute in 0.9% N/S only. Monitor glucose every 30 - 60 minutes at commencement.
Isoprenaline (inf)	0.02- 1 mcg/kg/min	0.2 mcg/kg/min	0.6 mg x wt	Neonates max 0.2 mcg/kg/min. Maximum for bradycardia 0.5mcg/kg/min. Up to 1mcg/kg/min for heart block. S/E Hypotension. Dilute in 5% dex or 0.9% N/S.
Ketamine (inf)	10-45 mcg/kg/min	10 mcg/kg/min	30 mg x wt	Anaesthetic, sialogogue. Hallucinations & emergence reactions worse in older children
Labetalol (inf)	0.5-3 mg/kg/hr	1 mg/kg/hr	50 mg x wt	Neonates start at 500mcg/kg/hr. Hypertensive crisis. Start slowly. Avoid rapid reduction BP. Dilute in 5% dex or 0.9% N/S.
Midazolam (inf)	0.5-20 mcg/kg/min	1 mcg/kg/min	3 mg x wt	Sedation at lower end of range. Seizure control higher doses. Cardiovascular depression. Dilute in 5% dex or 0.9% N/S.

Drug (inf = infusion)	*Dose range*	*1ml/hr =*	*Add to 50ml*	*Notes*
Milrinone (inf)	0.3-0.75 mcg/kg/min	0.5 mcg/kg/min	1.5 mg x wt	Phosphodiesterase inhibitor.Vasodilator & inotrope. Dose reduction in renal/ liver dysfunction. Dilute in 5% dex or 0.9% N/S. May be administered centrally undiluted in fluid restrcition.
Morphine (inf)	5-100 mcg/kg/hr	20 mcg/kg/hr	1 mg x wt	Bigger children may need higher doses for a few hours. Dilute in 5% dex or 0.9% N/S.
Noradrenaline (inf)	0.1-1 mcg/kg/min	0.1 mcg/kg/min	0.3 mg x wt	Dilute in 5% dex or 0.9% N/S. Potent vasopressor. Administer centrally
Propofol 1% (inf)	1-4 mg/kg/hr	10 mg/hr	0 mg x wt	1% = 1 kCal/ml in lipid. Use undiluted. Prolonged or high dose infusion associated with propofol syndrome (lactic acidosis and tachycardia)
Prostin (inf)	5- 100 ng/kg/min	10 ng/kg/min	30 mcg x wt	Dinoprostone. NANOGRAMS. Dosing up to 100ng/kg/min for 30-60 mins. Apnoea common in first 24hrs. S/E hypotension, flushing, diarrhoea, low grade temperature. Dilute in 5% dex or 0.9% N/S
Salbutamol (inf)	1-5 mcg/kg/min	0.5 mcg/kg/min	1.5 mg x wt	Dilute in 5% dex or 0.9% N/S. Preferable dilution is 25mg/50ml. Central administration if possible.
Sodium bicarbonate 8.4%(inf)	1-2 mmol/kg/hr	1 mmol/hr	0 mmol x wt	Renal alkalinisation . Very alkaline. High extravasation risk. Central administration preferable, Dilute 1:10 peripherally.
Sodium nitroprusside (inf)	1-5 mcg/kg/min	1 mcg/kg/min	3 mg x wt	Protect from light. Tachyphylaxis after 24 hrs. Toxicity with rising lactate and mixed venous saturations.
Thiopental (inf)	1-8 mg/kg/hr	1 mg/kg/hr	0 mg x wt	Reconstitute with 20ml WFI to give 25mg/ml. Further dilute with 0.9% N/S if required. Status epilepticus. Accumulates in fat. Cardiovascular suppression. Extravasation risk
Vasopressin (inf)	0.0001-0.002 unit/kg/min	0.0005 unit/kg/min	1.5 units x wt	Dosing range: low=0.0001u/kg/min; standard= 0.00025u/kg/min; high=0.0005u/kg/min; maz= 0.002u/kg/min. Dilute in 5% dex or 0.9% N/S.